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LEXICON  
GENETICS  
INC

2002 annual report



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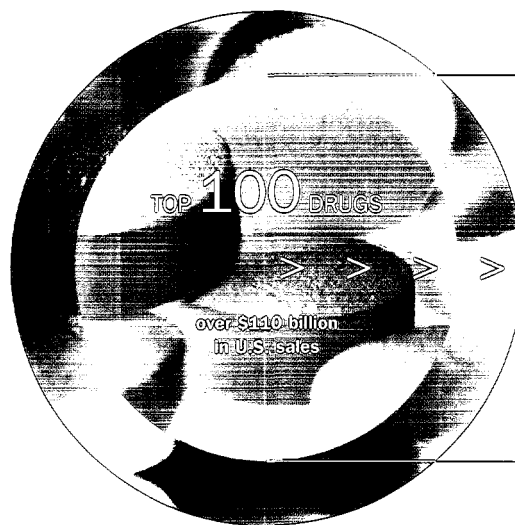
*inventing the*

NEXT  
GENERATION  
*of drugs*

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The top  
100 drugs  
address only

43

HUMAN  
TARGETS

*inventing* the NEXT GENERATION of drugs

*Lexicon Genetics* is a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are using gene knockout technology to systematically discover the physiological functions and pharmaceutical utility of genes. Our gene function discoveries fuel therapeutic development programs in diabetes, obesity, cardiovascular disease, immune disorders, neurological disease and cancer. We have established drug discovery alliances and functional genomics collaborations with leading pharmaceutical and biotechnology companies, research institutes and academic institutions throughout the world to commercialize our technology and turn our discoveries into drugs.

Lexicon's common stock is traded on the Nasdaq National Market under the ticker symbol LEXG.

mouse knockouts model drug action for **85%**  
of targets

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**34** OF  
HUMAN  
TARGETS  
have mouse knockouts

1 2 3 4 5 6 7 8 9 10 11 12 13  
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**29** OF  
model  
DRUG ACTION

## GENE KNOCKOUTS model top selling drugs

TARGET	INDICATION	SALES*	MOUSE PHYSIOLOGY
<b>Prilosec</b>	Gastroesophageal Reflux Disease	<b>\$5.7</b> billion in 2001 sales	Neutralization of stomach acid
<b>Procrit</b>	Anemia	<b>\$3.4</b> billion in 2001 sales	Failure to produce red blood cells
<b>Claritin</b>	Allergy	<b>\$3.2</b> billion in 2001 sales	Decreased immune, response, decreased alertness (drowsiness)
<b>Celebrex</b>	Arthritis	<b>\$3.1</b> billion in 2001 sales	Reduced inflammation, reduction in collagen- induced arthritis
<b>Prozac</b>	Depression	<b>\$2.0</b> billion in 2001 sales	Antidepressant behavior

\* Company reports

## financial highlights

(in thousands, except per share data)

Year ended December 31,

	2002	2001	2000
Revenues	\$ 35,200	\$ 30,577	\$ 14,459
Research and development expenses <sup>(1)</sup>	74,859	53,355	31,647
Loss from operations <sup>(2)</sup>	62,893	43,639	35,477
Interest and other income, net	3,223	8,467	9,483
Net loss attributable to common stockholders <sup>(2)</sup>	59,670	35,172	26,128
Pro forma net loss, excluding stock-based compensation <sup>(3)(4)</sup>	49,402	24,402	5,153
Net loss per share	1.14	0.70	0.63
Pro forma net loss per share, excluding stock-based compensation <sup>(3)(4)</sup>	0.95	0.49	0.11
Weighted average shares outstanding	52,263	50,213	41,618
Pro forma weighted average shares outstanding <sup>(4)</sup>	52,263	50,213	45,028

As of December 31,

	2002	2001	2000
Cash, cash equivalents and investments <sup>(5)</sup>	123,096	166,840	202,680
Stockholders' equity	169,902	218,372	207,628
Capital expenditures	19,766	13,471	7,709

<sup>(1)</sup> Includes non-cash, stock-based compensation of \$5,155, \$5,539 and \$10,883 in 2002, 2001 and 2000, respectively.

<sup>(2)</sup> Includes non-cash, stock-based compensation of \$10,268, \$10,770 and \$20,841 in 2002, 2001 and 2000, respectively.

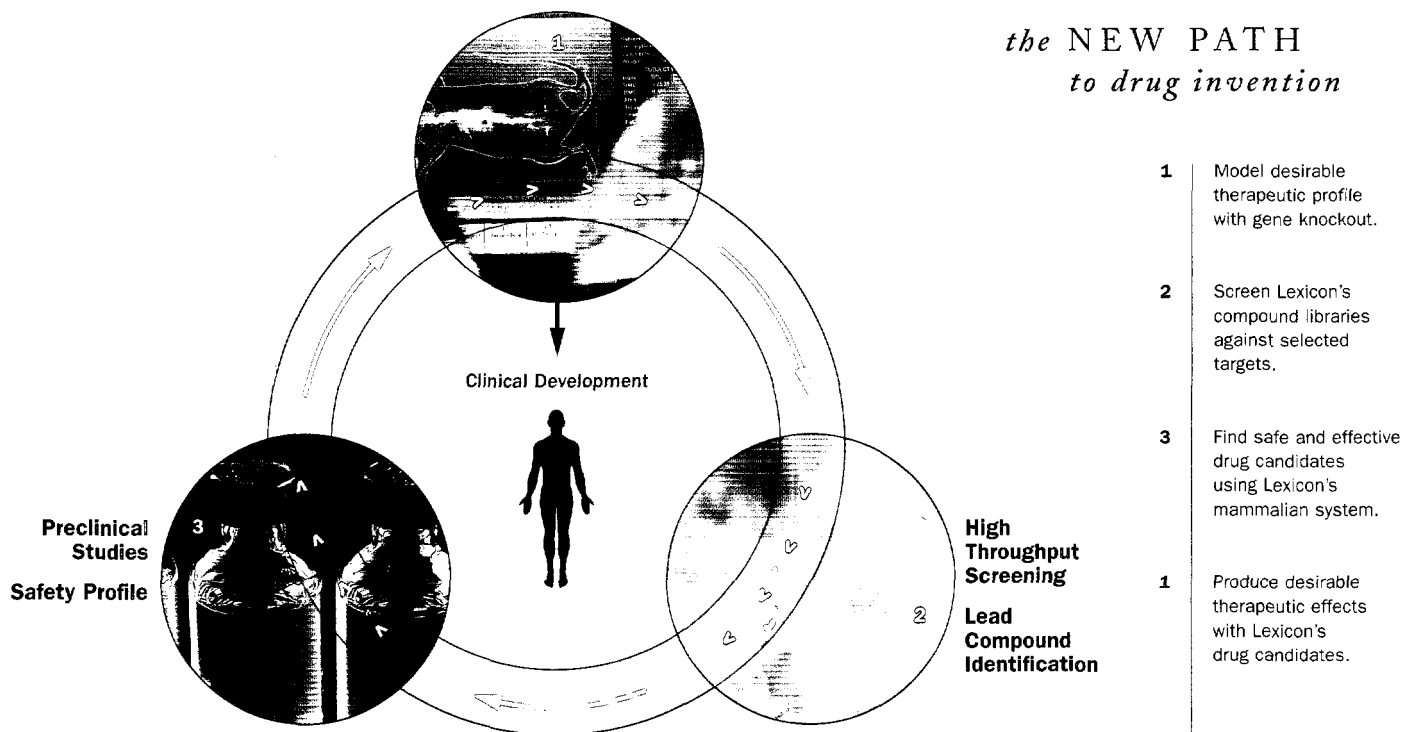
<sup>(3)</sup> Excludes non-cash, stock-based compensation of \$10,268, \$10,770 and \$20,841 in 2002, 2001 and 2000, respectively.

<sup>(4)</sup> Pro forma to reflect the April 2000 conversion of convertible preferred stock as if it had occurred at the beginning of the period and, in the case of pro forma net loss information, to exclude \$134 of accretion.

<sup>(5)</sup> Includes restricted cash and investments of \$57,710, \$43,338 and \$13,879 in 2002, 2001 and 2000, respectively.

Knockout Physiology >>> *in vivo* Efficacy

*the NEW PATH  
to drug invention*



*to our* **SHAREHOLDERS** 2002 was an exciting and highly productive year at Lexicon Genetics

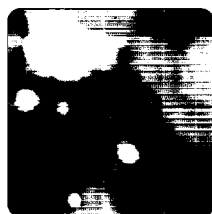
as we transformed our discoveries of the function of genes into drug discovery programs with breakthrough potential:

- We now have more than 15 drug discovery programs across five therapeutic areas;
- We discovered drug-like compounds for potential treatments in diabetes, obesity, atherosclerosis, autoimmune disease and organ transplant rejection;
- Genentech, Inc., makers of Rituxan and Herceptin, chose Lexicon to discover the medical use of new therapeutic proteins and antibody targets;
- We made significant progress in our alliances with Abgenix for the discovery of therapeutic antibodies and with Incyte for the discovery of therapeutic proteins;
- We increased our rate of discovery with the opening of the largest gene knockout generation and analysis facilities in the world;
- We were issued a new U.S. patent, broadening our patent estate in the field of gene trapping to six issued U.S. patents;
- We also received issuance of U.S. patents covering nine full-length sequences of potential drug targets identified in our gene discovery programs; and
- We grew revenues to \$35.2 million in 2002, marking the seventh consecutive year of revenue growth.

**INTERPRETING THE HUMAN GENOME FOR DRUG DISCOVERY** In 2002, the mouse genome was decoded, making it the second mammalian genome to be sequenced after that of the human. Each genome contains approximately 30,000 genes and, remarkably, 99% of human genes have similar mouse counterparts. Using the mouse as our guide, we have discovered key switches in physiology that have fueled Lexicon's drug discovery engine.

## LEXICON'S *drug discovery programs*

### CARDIOLOGY



Metabolic Syndrome  
Atherosclerosis  
Thrombosis

Cardiovascular diseases rank as the top killer in the United States according to the American Heart Association. 61.8 million Americans have some form of cardiovascular disease.

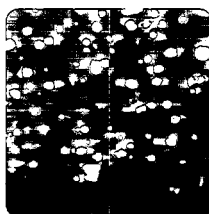
### IMMUNOLOGY



Transplantation  
Inflammation  
Autoimmune Disease

Arthritis and other rheumatic diseases are the number one cause of disability in the United States. According to the National Arthritis Action Plan, the economic impact of arthritis in this country is estimated at \$65 billion.

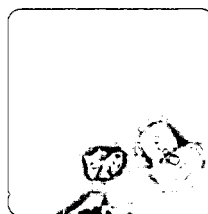
### NEUROLOGY



Depression  
Anxiety  
Cognition  
Pain

According to the National Institute of Mental Health, depressive disorders affect approximately 19 million American adults.

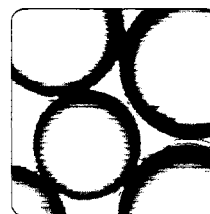
### CANCER



Solid Tumors

According to the American Cancer Society, cancer is the second leading cause of death in the United States, accounting for 1 of every 4 deaths. Since 1990, over 17 million new cancer cases have been diagnosed in the United States.

### METABOLISM



Diabetes  
Obesity  
Osteoporosis

Approximately 17 million people in the United States, or 6.2 percent of the population, have diabetes. Approximately 60 million adults in the United States are obese and 9 million severely obese.

**INVENTING A NEW GENERATION OF DRUGS** Lexicon's gene knockout technologies allow us to make reliable predictions of drug activity before the drugs are invented. This approach has been confirmed by a recent study of the top selling drugs in which we found that the therapeutic effect of drugs directly correlates with the physiology of mouse gene knockouts for approximately 85% of drug targets. Lexicon has taken the lead in applying the predictive power of gene knockout technology to invent the next generation of drugs.

We have completed the first 750 genes in our program to analyze 5,000 of the most promising genes for pharmaceutical discovery, and have already established drug discovery programs with breakthrough potential in each of our major disease areas. Using our industrialized gene knockout technology, Lexicon announced the discovery of seven additional drug discovery programs during 2002, including:

- **THROMBOSIS** – LG101. Inhibiting LG101 in mice resulted in a 60% reduction in blood clot formation with no observable, undesirable side effects;
- **INFLAMMATION** – LG688. We found that mice lacking LG688 had a 50% decrease in inflammatory response with no significant side effects;
- **OBESITY** – LG653. Mice with LG653 knocked out had a significant reduction in body fat, despite consuming more food, with no adverse side effects;
- **OBESITY** – LG747. Mice lacking the receptor LG747 had more than twice the body fat of normal animals, even at a young age, leading us to initiate a drug discovery program for the activation of that receptor;
- **CANCER** – LG152. We discovered that blocking LG152, prevalent in human breast and colon cancer cell lines, resulted in decreased cell growth and proliferation;

## "50 YEARS AGO

*the DNA double helix was first described by James Watson and Francis Crick, triggering a revolution in molecular biology. The next 50 years will focus on the molecular events that describe how genes control physiology and the genesis of disease. This new frontier will catalyze an exciting era of discovery not only of disease genes, but more importantly the next generation of breakthrough drugs."*

— Arthur T. Sands, M.D., Ph.D.



President and  
Chief Executive Officer  
ARTHUR T. SANDS, M.D., PH.D.

- **ATHEROSCLEROSIS**—LG914. Mice lacking LG914 maintained clear arteries in studies that normally result in significant arterial thickening without any observable, undesirable side effects; and
- **DEPRESSION**—LG527. Mice missing the LG527 gene showed an overall dramatic increase in activity levels and mobility with no on-target side effects observed.

**THE NEW PATH TO DRUG INVENTION** Using our strong chemistry platform at Lexicon Pharmaceuticals, we have moved our drug targets into medicinal chemistry. A year and a half after the formation of Lexicon Pharmaceuticals, we have successfully found multiple compounds for five of our drug discovery programs and are in the process of optimizing those compounds to select preclinical candidates in 2003. Having completed the expansion of Lexicon's drug discovery infrastructure, we anticipate moderating our growth in 2003, carefully preserving our cash for future investment in drug development.

We are turning our vision of discovering breakthrough treatments for human disease into reality. We firmly believe that our approach will result in a higher rate of success in drug discovery as we invent the next generation of drugs. It has been a year of great growth at Lexicon, and we look forward to new medical advances and pharmaceutical alliances in 2003 based on our rich harvest of breakthrough discoveries from the genome.

ARTHUR T. SANDS, M.D., PH.D.  
President and Chief Executive Officer

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 10-K

(Mark One)

- ☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2002

or

- ☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934

For the Transition Period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: 000-30111

Lexicon Genetics Incorporated

(Exact Name of Registrant as Specified in its Charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

76-0474169  
(I.R.S. Employer  
Identification Number)

8800 Technology Forest Place  
The Woodlands, Texas 77381  
(Address of Principal Executive  
Offices and Zip Code)

(281) 863-3000  
(Registrant's Telephone Number,  
Including Area Code)

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act:  
Common Stock, par value \$0.001 per share

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ☒ No ☐

The aggregate market value of voting stock held by non-affiliates of the registrant as of the last day of the registrant's most recently completed second quarter was approximately \$124.9 million, based on the closing price of the common stock on the Nasdaq National Market on June 28, 2002 of \$4.12 per share. For purposes of the preceding sentence only, all directors, executive officers and beneficial owners of ten percent or more of the registrant's common stock are assumed to be affiliates. As of March 10, 2003, 52,370,730 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2003 annual meeting of stockholders, which proxy statement will be filed under the Securities Exchange Act of 1934 within 120 days of the end of the registrant's fiscal year ended December 31, 2002, are incorporated by reference into Part III of this annual report on Form 10-K.

# Lexicon Genetics Incorporated

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The Lexicon name and logo, LexVision® and OmniBank® are registered trademarks and Genome5000™ and e-Biology™ are trademarks of Lexicon Genetics Incorporated.

In this annual report on Form 10-K, "Lexicon Genetics," "Lexicon," "we," "us" and "our" refer to Lexicon Genetics Incorporated.

### Factors Affecting Forward Looking Statements

This annual report on Form 10-K contains forward-looking statements. These statements relate to future events or our future financial performance. We have attempted to identify forward-looking statements by terminology including "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "should" or "will" or the negative of these terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Item 1. Business – Risk Factors," that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. We are not under any duty to update any of the forward-looking statements after the date of this annual report on Form 10-K to conform these statements to actual results, unless required by law.



## PART I

### Item 1. Business

#### Overview

Lexicon Genetics is a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are using gene knockout technology to systematically discover in living mammals, or *in vivo*, the physiological functions and pharmaceutical utility of genes. Our gene function discoveries fuel therapeutic discovery programs in diabetes, obesity, cardiovascular disease, immune disorders, neurological disease and cancer. We have established drug discovery alliances and functional genomics collaborations with leading pharmaceutical and biotechnology companies, research institutes and academic institutions throughout the world to commercialize our technology and turn our discoveries into drugs.

We generate our gene function discoveries using knockout mice – mice whose DNA has been altered to disrupt, or “knock out,” the function of the altered gene. Our patented gene trapping and gene targeting technologies enable us to rapidly generate these knockout mice by altering the DNA of genes in a special variety of mouse cells, called embryonic stem (ES) cells, which can be cloned and used to generate mice with the altered gene. We employ an integrated platform of advanced medical technologies to systematically discover and validate, *in vivo*, the physiological functions and pharmaceutical utility of the genes we have knocked out and the potential targets for therapeutic intervention, or drug targets, they encode.

We employ internal resources and drug discovery alliances to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We use our own sophisticated libraries of drug-like chemical compounds and an industrialized medicinal chemistry platform to identify small molecule drug candidates for our *in vivo*-validated drug targets. We have established alliances with Genentech, Inc. for the discovery of therapeutic proteins and antibody targets; with Abgenix, Inc. for the discovery and development of therapeutic antibodies based on our drug target discoveries; and with Incyte Genomics, Inc. for the discovery and development of therapeutic proteins. In addition, we have established collaborations and license agreements with many other leading pharmaceutical and biotechnology companies under which we receive fees and, in many cases, are eligible to receive milestone and royalty payments, in return for granting access to some of our technologies and discoveries for use in their own drug discovery efforts.

We believe that our industrialized approach of discovering and validating drug targets *in vivo*, together with our capabilities in small molecule drug discovery and the integration of our own capabilities with those of our alliance partners in therapeutic antibody and therapeutic protein discovery, will significantly increase our likelihood of success in discovering breakthrough treatments for human disease, and will reduce the risk, time and expense of discovering and developing therapeutics for new drug targets. Together, we believe that these factors will provide us with substantial strategic advantages in the competition to discover and develop genomics-based pharmaceutical products.

Lexicon Genetics was incorporated in Delaware in July 1995, and commenced operations in September 1995. Our corporate headquarters are located at 8800 Technology Forest Place, The Woodlands, Texas 77381, and our telephone number is (281) 863-3000.

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 are made available free of charge on our corporate website located at [www.lexicon-genetics.com](http://www.lexicon-genetics.com) as soon as reasonably practicable after the filing of those reports with the Securities and Exchange Commission. Information found on our website should not be considered part of this annual report on Form 10-K.

## Key Milestones and Achievements in 2002

We made substantial business and technical progress in 2002:

- We continued to advance additional *in vivo*-validated drug targets into therapeutic discovery programs, and identified compounds demonstrating activity in several of our more advanced programs;
- We established an alliance with Genentech for the discovery of therapeutic proteins and antibody targets;
- We made further progress in our alliances with Abgenix for the discovery of therapeutic antibodies and with Incyte for the discovery of therapeutic proteins;
- We granted non-exclusive, internal research-use sublicenses under our gene targeting patents to Genentech, Biogen, Inc. and Millennium Pharmaceuticals, Inc.;
- We obtained an additional key patent covering our gene trapping technology, as well as patents covering nine full-length sequences of potential drug targets identified in our gene discovery programs;
- We brought on-line our new office, laboratory and animal facilities;
- We substantially increased our rate of productivity in our Genome5000 program for the discovery of the *in vivo* functions of 5,000 genes over five years, ending the year having completed the analysis of the functions of 750 genes; and
- We achieved more than \$35 million in revenues, marking our seventh consecutive year of revenue growth.

We believe we are poised to capitalize on these achievements in 2003 by further accelerating the pace of our Genome5000 program, substantially expanding our pipeline of *in vivo*-validated drug targets, advancing our therapeutic discovery programs towards clinical development, and establishing additional drug discovery alliances and functional genomics collaborations to commercialize our technology and further develop our discoveries.

## Genomics and Drug Discovery

### *The Human Genome*

The human genome is comprised of complementary strands of deoxyribonucleic acid, or DNA, molecules organized into 23 pairs of chromosomes. Genes, which carry the specific information, or code, necessary to construct, or express, the proteins that regulate human physiology and disease, make up approximately two to four percent of the genome. The remaining 96% to 98% of DNA in chromosomes does not code for protein. Although estimates vary as to the total number of genes within the total of approximately three billion nucleotide base pairs of "genomic" or "chromosomal" DNA that make up the human genome, it is estimated that the human genome contains approximately 30,000 genes.

The Human Genome Project and other publicly and privately-funded DNA sequencing efforts invested considerable resources to sequence the genes in the human genome, culminating in the completion of a "working draft" of sequence from the human genome in the year 2000 and its publication in February 2001. The sequence of a gene alone, however, does not permit reliable predictions of its function in physiology and disease. As a result, the databases of gene sequences generated by these efforts can be compared by analogy to a dictionary that contains thousands of words, but only a handful of definitions.

### *Functional Genomics*

The efforts to discover these definitions – to define the functions of the genes in the human genome and, in doing so, discover which genes encode pharmaceutically valuable drug targets – are commonly referred to as

functional genomics. Researchers use a variety of methods to obtain clues about gene function, such as gathering information about where a gene's transcript is found and where the corresponding protein is expressed in the cell, and conducting experiments using cell culture, biochemical studies and non-mammalian organisms. While these methods may provide useful information about gene function at the biochemical and cellular levels, their ability to provide information about how genes control mammalian physiology, and thus their usefulness for drug discovery and development, is significantly limited.

We believe that the method for defining gene function that has the greatest relevance and highest value for drug discovery is to disrupt, or knock out, the gene in a mouse and assess the resulting physiological, pathological and behavioral consequences. As mammals, humans and mice have very similar genomes and share very similar physiology – one of the reasons that mice are among the most widely used animal model systems in the pharmaceutical industry. As a result of these similarities, the *in vivo* analysis of the function of a gene in knockout mice – mice whose DNA has been altered to disrupt, or “knock out,” the function of the altered gene – enables the predictions to be made regarding the effects on human physiology of prospective therapeutics that modulate the corresponding human drug target and, therefore, regarding the pharmaceutical utility and value of the target for the discovery and development of such therapeutics.

### *Genomics-Based Drug Discovery*

We believe that genomics represents a significant opportunity for the discovery and development of breakthrough treatments for human disease. Drugs on the market today interact with a total of about 120 specific protein targets, each of which is encoded by a gene. Of those, only 43 represented human host proteins targeted by one or more of the 100 best-selling drugs of 2001. While estimates of the total number of potential drug targets encoded within the human genome vary, some experts believe that genomics research could discover as many as 5,000 new targets for pharmaceutical development. Our own experience suggests that the number of new targets with true pharmaceutical value is much lower, perhaps in the range of 100 to 150 new high-quality targets. This would still be a substantial increase from the number of targets that fuel the pharmaceutical industry at present, but demonstrates the importance of selecting the drug targets with the greatest pharmaceutical utility from the much larger pool of potential targets. The fact that very little is known about the physiological functions of most genes, however, presents a major challenge in making these selections, and for drug discovery research generally, which has traditionally relied primarily on established drug targets with well-characterized functions.

The magnitude of this challenge is evident in expectations regarding the productivity of drug discovery research for genomics-based drug targets. According to the *Fruits of Genomics*, a 2001 study conducted by McKinsey & Co. and Lehman Brothers, the average cost of bringing a single drug to market, estimated at \$800 million in 2000, may increase to as much as \$1.6 billion by 2005. The primary driver of the increase is the expected change, as a result of the wealth of potential drug targets generated by the Human Genome Project and other publicly and privately-funded DNA sequencing efforts, in the proportion of drug targets in pharmaceutical companies' research pipelines that are “unprecedented” – that is, drug targets for which therapeutics have not previously been developed. The study estimates that this increase in unprecedented drug targets will result in substantially higher rates of failure in early preclinical biological validation and Phase 2 clinical development.

The chief cause of these failures, we believe, is the advancement of unprecedented drug targets into expensive screening and therapeutic discovery programs without an understanding of the *in vivo* biology and physiological function of the target. Because target selection decisions drive all subsequent drug discovery and development spending, and failures account for 75% or more of the average cost of bringing a drug to market, the quality of target selection decisions has a disproportionate effect on the overall cost of bringing a drug to market.

### *Our Strategy*

We believe that the discovery and selection of drug targets that have high pharmaceutical value – that exhibit favorable therapeutic profiles and address large medical markets – will be the key determinant of success in genomics-based drug discovery. The solution to this challenge, we believe, requires redefining the way drug discovery is conducted by systematically determining the physiological functions of large numbers of genes in mice, which, as mammals, share significant genetic and physiological similarities with humans. We believe that the resulting information will enable us to discover which potential targets from the human genome exhibit favorable

therapeutic profiles and address large medical markets. In addition, we believe that identifying these drug targets at the very beginning of the drug discovery process, before committing to expensive screening and therapeutic discovery programs, will substantially increase the productivity and cost-effectiveness of our drug discovery efforts relative to other approaches. Together, we believe that these factors will significantly increase our likelihood of success in discovering breakthrough treatments for human disease, and will reduce the risk, time and expense of discovering and developing therapeutics for new drug targets.

Our principal objective is to establish a leadership position in the discovery of breakthrough treatments for human disease. The key elements of our strategy include the following:

- systematically discover, *in vivo*, the physiological functions and pharmaceutical utility of 5,000 genes over five years in our Genome5000 program;
- employ internal resources and drug discovery alliances to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for *in vivo*-validated drug targets that we consider to have high pharmaceutical value;
- develop promising therapeutic candidates through drug development alliances or with our own resources; and
- generate near-term revenues through collaborations and license agreements with pharmaceutical and biotechnology companies in return for granting access to some of our technologies and discoveries for use in their own drug discovery efforts.

#### Our Technology Platform

We have developed, refined and integrated a technology platform that spans the drug discovery process from gene identification to the discovery and development of therapeutics, with a focus on the systematic discovery and validation, *in vivo*, of the physiological functions and pharmaceutical utility of genes and the drug targets they encode, and the discovery and development of therapeutics for our *in vivo*-validated drug targets. Our technology platform includes both proprietary and non-proprietary technologies in gene sequencing and discovery, bioinformatics analysis, expression analysis, gene knockouts, biological and physiological analysis, chemical compound libraries, assay development, high-throughput screening and medicinal chemistry.

The core elements of our technology platform include our patented technologies for the generation of gene knockouts, our integrated platform of advanced medical technologies for the systematic and comprehensive biological analysis of *in vivo* physiology, and our industrialized approach to medicinal chemistry and the generation of high-quality, drug-like compound libraries. These core elements of our technology platform are described below.

#### Gene Knockout Technologies

We have developed and refined gene knockout technologies and expertise to rapidly and efficiently generate knockout mice for the *in vivo* analysis of the physiological functions of thousands of genes. Our patented gene trapping and gene targeting technologies, our experience in using these technologies and the scale of our gene knockout operations provide us with substantial advantages over the methods generally used to generate knockout mice, allowing us to overcome limitations inherent in such methods that restrict the rate at which knockout mice may be produced and, therefore, the rate at which the genes in the mammalian genome may be analyzed.

**Gene Targeting.** Our gene targeting technology, which is covered by six issued patents, enables us to generate highly-specific alterations in targeted genes. The technology uses a vector to replace DNA of a gene in a mouse ES cell with DNA from the targeting construct in the chromosome of the cell through a process known as homologous recombination. When used to knock out a gene, the DNA from the targeting construct disrupts the function of the targeted gene, permitting the generation of knockout mice.

We use our gene targeting technology to knock out the function of the targeted gene for the analysis of the gene's function. We also use this technology in combination with one or more additional technologies such as *Cre/lox* recombinase technology to generate alterations that selectively disrupt, or conditionally regulate, the function of the targeted gene for the analysis of the gene's function in selected tissues, at selected stages in the animal's development or at selected times in the animal's life. In addition, we can use this technology to replace the targeted gene with its corresponding human gene, or ortholog, for use in our therapeutic discovery programs.

We have developed an industrialized approach to gene targeting, and believe that our experience using this technology and the scale of our gene targeting operations provide us with substantial advantages in efficiency and speed relative to others using similar approaches to generate knockout mice.

*Gene Trapping.* Our gene trapping technology, which is covered by six issued patents, is a high-throughput method of generating knockout mouse clones that we invented. The technology uses genetically engineered retroviruses that infect mouse ES cells *in vitro*, integrate into the chromosome of the cell and deliver molecular traps for genes. The gene trap disrupts the function of the gene into which it integrates, permitting the generation of knockout mice. The gene trap also stimulates transcription of a portion of the trapped gene, using the cell's own splicing machinery to extract this transcript from the chromosome for automated DNA sequencing. This allows us to identify and catalogue each ES cell clone by DNA sequence from the trapped gene, and to select ES cell clones by DNA sequence for the generation of knockout mice.

We have used our gene trapping technology in an automated process to create our OmniBank library of more than 200,000 frozen gene knockout ES cell clones, each identified by DNA sequence in a relational database. Because our gene trapping vectors are designed to trap genes in a manner largely independent of their levels of expression, our OmniBank library includes even those genes that are very rarely expressed. We estimate that our OmniBank library currently contains gene knockout clones for more than half of all genes in the mammalian genome.

We believe our OmniBank library, which is by far the largest library of gene knockout clones in the world, provides us with unparalleled strategic advantages in the discovery of *in vivo* gene function. The OmniBank library permits us to generate knockout mice for *in vivo* analysis at a significantly higher rate than is possible using other methods. We have generated many of our *in vivo*-validated drug target discoveries that we consider to have high pharmaceutical value using knockout mice generated from our OmniBank library.

#### *Physiological Analysis Technologies*

We have assembled and integrated a technology platform for *in vivo* physiological analysis using a medical center approach to genes, enabling us to systematically define the functions and pharmaceutical utility of the genes we have knocked out and the potential targets for therapeutic intervention, or drug targets, they encode.

*Gene Function Discovery.* We employ an integrated platform of advanced medical technologies to rapidly and systematically discover and catalogue the functions of the genes we have knocked out using our gene trapping and gene targeting technologies. These technologies include many of the most sophisticated diagnostic technologies that might be found in a major medical center, from CAT-scans and magnetic resonance imaging (MRI) to complete blood cell analysis, all adapted specifically for the analysis of mouse physiology. This state-of-the-art technology platform enables us to assess the phenotypic consequences, or function in a living mammal, of the knocked-out gene across a variety of parameters relevant to human disease, including cancer, cardiovascular disease, immune disorders, neurological disease, diabetes and obesity. Most of the technologies we employ are non-invasive, permitting longitudinal studies of gene function over time that are not feasible using conventional techniques for the analysis of knockout mice. The information resulting from this analysis is captured in relational databases for our use, and use by our collaborators, in drug discovery.

We believe that our medical center approach and the technology platform that makes it possible provide us with substantial advantages over other approaches to gene function and drug target discovery. We believe that our comprehensive, unbiased approach allows us to uncover functions within the context of mammalian physiology that might be missed by more narrowly-focused efforts directed on the basis of hypotheses as to the gene's likely function, particularly when these hypotheses are based on expression analyses and other factors that our experience

indicates are unreliable predictors of gene function. We also believe our approach is more likely to uncover target-related side effects that might limit the utility of potential therapeutics addressing the drug target or prove to be unacceptable in light of the potential therapeutic benefit. In both these cases, we believe these advantages will contribute to better target selection and, therefore, to the success of our drug discovery and development efforts.

*Preclinical Analysis of Therapeutic Candidates.* We employ the same physiological analysis technology platform that we use in the discovery of gene function to analyze the *in vivo* efficacy and safety profiles of therapeutic candidates in mice. We believe that this approach will allow us, at an early stage, to identify and optimize therapeutic candidates for further preclinical and clinical development that demonstrate superior *in vivo* efficacy and to distinguish compound-related effects from the target-related effects that we defined using the same systematic, comprehensive series of tests. The result, we believe, will substantially increase our likelihood of success in traditional preclinical and clinical development, and will reduce the risk, time and expense of developing our therapeutics for our *in vivo*-validated drug targets.

### *Medicinal Chemistry Technology*

We acquired state-of-the-art medicinal chemistry capabilities through our July 2001 acquisition of Coelacanth Corporation, which forms the foundation of our Lexicon Pharmaceuticals division focused on the discovery and development of small molecule drugs for our *in vivo*-validated drug targets. We use solution-phase chemistry to generate diverse libraries of optically pure compounds that are targeted against the same categories of drug targets we address in our Genome 5000 drug target discovery program. We design these libraries by analyzing the chemical structures of drugs that have been proven safe and effective against human disease and synthesizing that knowledge in the design of scaffolds and chemical building blocks for the generation of large numbers of new drug-like compounds. These building blocks, which we refer to as "pharmacophoric modules," can rapidly be reassembled to generate optimization libraries when we identify a hit, or compound demonstrating activity, against one of our *in vivo*-validated targets, enabling us to rapidly optimize those hits and accelerate our medicinal chemistry efforts.

### *Research and Development Programs*

#### *Genome5000 Drug Target Discovery Program*

We are using our industrialized approach to gene targeting and our OmniBank library of more than 200,000 gene knockout ES cell clones, together with our integrated platform of advanced physiological analysis technologies, to systematically discover in living mammals, or *in vivo*, the functions and pharmaceutical utility of a total of 5,000 genes over five years in our Genome5000 program. The Genome5000 program includes the 1,250 drug targets that we have committed to include in our LexVision database of *in vivo*-validated drug targets, as well as the additional drug targets that we are pursuing in internal programs and drug discovery alliances. We believe that our *in vivo* validation of the drug targets discovered in our Genome5000 program provides us and our collaborators with substantial advantages over competing validation approaches in the discovery and development of genomics-based pharmaceutical products.

Our Genome5000 efforts are focused on the discovery of the functions in mammalian physiology of proteins encoded by pharmaceutically important gene families, such as G-protein coupled (GPCRs) and other receptors, kinases, ion channels, other key enzymes and secreted proteins. We use bioinformatics analysis and other resources to prioritize genes for analysis in this program from a variety of sources, including our own proprietary gene sequence databases, which encompass hundreds of full-length human gene sequences and more than 50,000 partial human gene sequences that we discovered using our gene trapping technology, our OmniBank database and library, Incyte's LifeSeq<sup>®</sup> Gold Database and the public human genome project.

We have identified *in vivo*-validated drug targets in each of our internal disease biology programs, which include programs for the identification of drug targets with pharmaceutical utility in the discovery of therapeutics for the treatment of diabetes, obesity, cardiovascular disease, immune disorders, neurological disease and cancer. We are moving many of these targets forward into therapeutic discovery and development programs, both on our own and with collaborators.

### *Therapeutic Discovery Programs*

We employ internal resources and drug discovery alliances to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We use our own sophisticated libraries of drug-like chemical compounds and an industrialized medicinal chemistry platform to identify small molecule drug candidates for our *in vivo*-validated drug targets. We have established alliances with Genentech for the discovery of therapeutic proteins and antibody targets; with Abgenix for the discovery and development of therapeutic antibodies based on our drug target discoveries; and with Incyte for the discovery and development of therapeutic proteins.

Our criteria for advancing *in vivo*-validated drug targets into therapeutic discovery and development programs include the following:

- *Favorable Therapeutic Profile.* The drug target must demonstrate a favorable therapeutic profile *in vivo*. Specifically, our *in vivo* analysis must suggest that the effect of inhibiting or otherwise modulating the activity of the drug target in humans would have a therapeutic effect in treating disease, with an acceptable target-related side effect profile.
- *Novel Function.* The function of the drug target must be novel – that is, we are interested in drug targets whose function was not generally known to others before we discovered it.
- *Large Medical Market.* The potential market for therapeutics addressing the drug target must be substantial. We are interested in drug targets that are key switches that control human physiology, addressing large markets such as heart disease, diabetes, depression and cancer.

Our small molecule drug discovery programs involve the following stages:

- assay development and high throughput screening (HTS) to identify “hits,” or compounds demonstrating activity, against the *in vivo*-validated targets;
- medicinal chemistry efforts to optimize the potency and selectivity of the hits, to identify lead compounds for further development;
- lead optimization and preliminary preclinical analysis;
- formal preclinical studies of optimized leads; and
- clinical development.

Our most advanced projects to date have reached the lead optimization and preliminary preclinical analysis stage.

As of March 10, 2003, we had advanced more than 15 *in vivo*-validated drug targets into therapeutic discovery programs.

### *Research and Development Expenses*

In 2002, 2001 and 2000, respectively, we incurred expenses of \$74.9 million, \$53.4 million and \$31.6 million in company-sponsored research and development activities, including \$5.2 million, \$5.5 million and \$10.9 million, respectively, of stock-based compensation expense.

## Collaborations and Alliances

Our collaboration and alliance strategy involves:

- drug discovery alliances to discover and develop therapeutics based on our drug target discoveries, particularly when the alliance enables us to obtain access to technology and expertise that is complementary to our own; and
- functional genomics collaborations with pharmaceutical and biotechnology companies, research institutions and academic institutions to generate near-term revenues for granting access to some of our technologies and discoveries for use in their own drug discovery efforts, as well as the potential, in many cases, for milestone payments and royalties on products they develop using our technology.

In implementing this strategy, we have entered into the drug discovery alliances and functional genomics collaborations with leading pharmaceutical and biotechnology companies, research institutions and academic institutions throughout the world, as described below.

### *Drug Discovery Alliances*

We have entered into the following alliances for the discovery and development of therapeutics based on our *in vivo* drug target discovery efforts:

*Genentech, Inc.* We established a drug discovery alliance with Genentech in December 2002 to discover novel therapeutic proteins and antibody targets. Under the alliance agreement, we will use our functional genomics technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Genentech will have exclusive rights in the discoveries resulting from the collaboration for the research, development and commercialization of therapeutic proteins and antibodies. We will retain certain other rights in those discoveries, including rights for the development of small molecule drugs. We received an up-front payment and will receive performance payments for our work in the collaboration as it is completed. We will also receive milestone payments and royalties on sales of therapeutic proteins and antibodies for which Genentech obtains exclusive rights. The agreement has an expected collaboration term of three years.

*Abgenix, Inc.* We established a drug discovery alliance with Abgenix in July 2000 to discover novel therapeutic antibodies using our functional genomics technologies and Abgenix's technology for generating fully human monoclonal antibodies. We and Abgenix expanded and extended the alliance in January 2002, with the intent of accelerating the selection of *in vivo*-validated antigens for antibody discovery and the development and commercialization of therapeutic antibodies based on those targets. Under the alliance agreement, we and Abgenix will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic antibodies, and will each receive milestone payments and royalties on sales of therapeutic antibodies from the alliance that are commercialized by the other party or a third party sublicensee. Each party will bear its own expenses under the alliance. The expanded alliance also provides us with access to Abgenix's XenoMouse® technology for use in some of our own drug discovery programs. The agreement, as extended, has a term of four years, subject to the right of the parties to extend the term for up to three additional one-year periods.

*Incyte Genomics, Inc.* We established a drug discovery alliance with Incyte in June 2001 to discover novel therapeutic proteins using our functional genomics technologies in the discovery of the functions of secreted proteins from Incyte's LifeSeq® Gold database. Under the alliance agreement, we and Incyte will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic proteins, and will each receive milestone payments and royalties on sales of therapeutic proteins from the alliance that are commercialized by the other party or a third party sublicensee. The agreement has a term of five years, although either party may terminate the agreement after three years.



### *LexVision Collaborations*

We have entered into the following collaborations for access to our LexVision database of *in vivo*-validated drug targets:

*Bristol-Myers Squibb Company.* We established a LexVision collaboration with Bristol-Myers Squibb in September 2000, under which Bristol-Myers Squibb has non-exclusive access to our LexVision database and OmniBank library for the discovery of small molecule drugs. We receive access fees under this agreement, and are entitled to receive milestone payments and royalties on products Bristol-Myers Squibb develops using our technology. The agreement has a term of five years, although either party may terminate the agreement after three years.

*Incyte Genomics, Inc.* We established a LexVision collaboration with Incyte in June 2001, under which Incyte has non-exclusive access to our LexVision database and OmniBank library for the discovery of small molecule drugs. We receive access fees under this agreement, and are entitled to receive milestone payments and royalties on products Incyte develops using our technology. The agreement has a term of five years, although either party may terminate the agreement after three years.

### *Functional Genomics Collaborations*

We have established functional genomics collaboration agreements with a number of leading pharmaceutical and biotechnology companies for the generation and, in some cases, analysis of knockout mice for genes requested by the collaborator. Under these agreements, we grant non-exclusive licenses to the collaborator for use in its internal drug discovery programs of the knockout mice and, if applicable, analysis data that we generate under the agreement. Some of these agreements also provide for non-exclusive access to our OmniBank database. We typically receive annual subscription fees and fees for knockout mice with annual minimum commitments and, under some of these agreements, may receive royalties on products that our collaborators discover or develop using our technology.

We have entered into functional genomics collaboration agreements with the following companies:

<u>Company</u>	<u>Date of Agreement</u>	<u>End of Access Period</u>
Amgen, Inc.	July 2001	July 2003
Abgenix, Inc.	January 2001	January 2004
Tularik Inc.	October 2000	October 2003
Wyeth	March 2000	March 2003
Boehringer Ingelheim Pharmaceuticals, Inc.	February 2000	February 2004
Pharmacia Corp.	January 2000	January 2003
Johnson & Johnson Pharmaceutical Research and Development L.L.C.	December 1999	December 2003
N.V. Organon	December 1999	December 2002
Millennium Pharmaceuticals, Inc.	July 1999	June 2002

Each of these agreements has a specified access period during which the collaborator may request new projects, although we continue to conduct work and the agreement remains in effect until the projects requested during the access period are completed.

We have also entered into functional genomics collaboration agreements with a number of additional companies and academic institutions throughout the world under which we receive research fees for the generation of knockout mice and, with participating institutions, certain rights to license inventions or royalties on products discovered using such mice.

### *e-Biology Global Collaboration Program*

We believe that our OmniBank database and library represent a unique resource for catalyzing collaborations with researchers at pharmaceutical companies, biotechnology companies and academic institutions

for the discovery of gene function. We provide access to our OmniBank database through the Internet to subscribing researchers at leading companies and academic institutions throughout the world. Our bioinformatics software allows subscribers to mine our OmniBank database for genes of interest, and we permit subscribers to acquire OmniBank knockout mice or ES cells on a non-exclusive basis for the determination of gene function under our e-Biology collaboration program. In this program, we receive fees for OmniBank knockout mice and, with participating institutions, rights to license inventions or to receive royalties on pharmaceutical products discovered using our mice. In cases where we do not obtain such rights, our e-Biology collaborations leverage the value of OmniBank since we retain rights to use the same OmniBank knockout mice in our own gene function research and with commercial collaborators. We have more than 100 agreements under our e-Biology collaboration program with researchers at leading institutions throughout the world.

#### Technology Licenses and Compound Sales

In addition to collaborations, we have used technology licenses and compound library sales to generate revenues for the support of our own research and development efforts.

*Technology Licenses.* We have granted non-exclusive, internal research-use sublicenses under certain of our gene targeting patent rights to a total of 12 leading pharmaceutical and biotechnology companies. Many of these agreements have terms of one to three years, in some cases with provisions for subsequent renewals. Others extend for as long as the life of the patents. We typically receive up-front license fees and, in some cases, receive additional license fees or milestone payments on products that the sublicensee discovers or develops using our technology.

*Compound Library Sales.* Our Lexicon Pharmaceuticals subsidiary has entered into agreements with a total of 29 leading pharmaceutical and biotechnology companies for non-exclusive access to selected compound libraries. Most of these agreements were completed by Coelacanth prior to our July 2001 acquisition of the company. The remainder were completed in 2001 as we wound down Coelacanth's compound sales efforts in support of our strategic decision to use our compound libraries principally in our own drug discovery efforts. These agreements typically provide for our sale of compounds from the selected library for use by the customer in its own internal drug discovery efforts. Under some of these agreements, we have agreed to provide additional quantities of selected compounds or optimization services in exchange for further payments. Subject to limited exceptions, we do not intend to continue to make our compound libraries available for purchase in the future.

#### Patents and Proprietary Rights

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that those rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Accordingly, patents and other proprietary rights are an essential element of our business. We seek patent protection for the genes, proteins and drug targets that we discover. Specifically, we seek patent protection for:

- the sequences of genes that we believe to be novel, including full-length genes and the partial gene sequences contained in our human gene trap and OmniBank databases, the proteins they encode and their predicted utility as a drug target or therapeutic protein;
- the utility of genes and the drug targets or therapeutic proteins they encode based on our discoveries of their biological functions using knockout mice;
- drug discovery assays for our *in vivo*-validated targets;
- chemical compounds and their use in treating human diseases and conditions; and
- various enabling technologies in the fields of mutagenesis, ES cell manipulation and transgenic or knockout mice.

We own or have exclusive rights to six issued U.S. patents that cover our gene trapping technology, nine issued U.S. patents that cover full-length sequences of potential drug targets identified in our gene discovery

programs, and five issued U.S. patents that cover specific knockout mice and discoveries of the functions of genes made using knockout mice. We have licenses under 47 additional U.S. patents, and corresponding foreign patents and patent applications, in the fields of gene targeting, gene trapping and genetic manipulation of mouse ES cells. These include patents to which we hold exclusive rights in certain fields, including a total of six U.S. patents covering the use of positive-negative selection and isogenic DNA gene targeting technology, as well as patents covering the use of Cre/lox technology. We have filed or have exclusive rights to more than 500 pending patent applications in the United States Patent and Trademark Office, the European Patent Office, the national patent offices of other foreign countries or under the Patent Cooperation Treaty, covering our gene trapping technology, the DNA sequences of genes, the utility of drug targets, drug discovery assays, and other products and processes. Collectively, these patent applications cover, among other things, approximately 200 full-length human gene sequences, more than 50,000 partial human gene sequences, and more than 45,000 knockout mouse clones and corresponding mouse gene sequence tags. Patents typically have a term of no longer than 20 years from the date of filing.

All of our employees, consultants and advisors are required to execute a confidentiality agreement upon the commencement of employment or consultation. In general, the agreement provides that all inventions conceived by the employee or consultant, and all confidential information developed or made known to the individual during the term of the agreement, shall be our exclusive property and shall be kept confidential, with disclosure to third parties allowed only in specified circumstances. We cannot assure you, however, that these agreements will provide useful protection of our proprietary information in the event of unauthorized use or disclosure of such information.

### **Competition**

The biotechnology and pharmaceutical industries are highly competitive and characterized by rapid technological change. We face significant competition in each of the aspects of our business from for-profit companies such as Human Genome Sciences, Inc., Millennium Pharmaceuticals, Inc. and Exelixis, Inc., among others, many of which have substantially greater financial, scientific and human resources than we do. In addition, the Human Genome Project and a large number of universities and other not-for-profit institutions, many of which are funded by the U.S. and foreign governments, are also conducting research to discover genes and their functions.

While we are not aware of any other commercial entity that is developing large-scale gene trap mutagenesis in ES cells, we face significant competition from entities using traditional knockout mouse technology and other technologies. Several companies, including Deltagen, Inc. and DNX (a subsidiary of Xenogen Corporation), and a large number of academic institutions create knockout mice for third parties using these more traditional methods, and a number of companies create knockout mice for use in their own research.

Many of our competitors in drug discovery and development have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we have. As a result, our competitors may succeed in developing products earlier than we do, obtaining approvals from the FDA or other regulatory agencies for those products more rapidly than we do, or developing products that are more effective than those we propose to develop. Similarly, our collaborators face similar competition from other competitors who may succeed in developing products more quickly, or developing products that are more effective, than those developed by our collaborators. We expect that competition in this field will intensify.

### **Government Regulation**

#### *Regulation of Pharmaceutical Products*

The development, production and marketing of any pharmaceutical products developed by us or our collaborators will be subject to extensive regulation by United States and foreign governmental authorities. In the United States, new drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act and biological products are subject to regulation both under certain provisions of that Act and under the Public Health Services Act. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of drugs and biologics. The process of obtaining FDA approval has historically been costly and time-consuming.

The standard process required by the FDA before a pharmaceutical product may be marketed in the United States includes:

- preclinical tests;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug or biologic in our intended application;
- for drugs, submission of a New Drug Application, or NDA, and, for biologics, submission of a Biologic License Application, or BLA, with the FDA; and
- FDA approval of the NDA or BLA prior to any commercial sale or shipment of the product.

In addition to obtaining FDA approval for each product, each drug or biologic manufacturing establishment must be inspected and approved by the FDA. All manufacturing establishments are subject to inspections by the FDA and by other federal, state and local agencies and must comply with current Good Manufacturing Practices requirements.

Preclinical studies can take several years to complete, and there is no guarantee that an IND based on those studies will become effective to even permit clinical testing to begin. Once clinical trials are initiated, they generally take four to seven years, but may take longer, to complete. After completion of clinical trials of a new drug or biologic product, FDA marketing approval of the NDA or BLA must be obtained. This process requires substantial time and effort and there is no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that approval will be granted. In the past, the FDA's approval of the NDA or BLA has taken, on average, one to three years; if questions arise, approval can take longer.

In addition to regulatory approvals that must be obtained in the United States, a drug product is also subject to regulatory approval in other countries in which it is marketed, although the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary widely from country to country. No action can be taken to market any drug product in a country until an appropriate application has been approved by the regulatory authorities in that country. FDA approval does not assure approval by other regulatory authorities. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In some countries, the sale price of a drug product must also be approved. The pricing review period often begins after market approval is granted. Even if a foreign regulatory authority approves a drug product, it may not approve satisfactory prices for the product.

#### *Other Regulations*

In addition to the foregoing, our business is and will be subject to regulation under various state and federal environmental laws, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in and wastes generated by our operations. We believe that we are in material compliance with applicable environmental laws and that our continued compliance with these laws will not have a material adverse effect on our business. We cannot predict, however, whether new regulatory restrictions on the production, handling and marketing of biotechnology products will be imposed by state or federal regulators and agencies or whether existing laws and regulations will not adversely affect us in the future.

#### *Employees and Consultants*

We believe that our success will be based on, among other things, achieving and retaining scientific and technological superiority and identifying and retaining capable management. We have assembled a highly qualified team of scientists as well as executives with extensive experience in the biotechnology industry.

As of March 3, 2003, we employed 579 persons, of whom 123 hold M.D., Ph.D. or D.V.M. degrees and another 123 hold other advanced degrees. We believe that our relationship with our employees is good.

#### Scientific Advisory Panel Members

We have consulting relationships with a number of scientific advisors. At our request, these advisors review the feasibility of product development programs under consideration, provide advice concerning advances in areas related to our technology and aid in recruiting personnel. Most of these advisors receive cash and stock-based compensation for their services, and in some cases receive access to our OmniBank database and mice from our OmniBank library. Most of these advisors are employed by academic institutions or other entities and may have commitments to or advisory agreements with other entities that may limit their availability to us. Our advisors are required to disclose and assign to us any ideas, discoveries and inventions they develop in the course of providing consulting services to us. We also use consultants for various administrative needs. None of our consultants or advisors is otherwise affiliated with us.

Our scientific advisors and consultants include the following persons:

<u>Name</u>	<u>Affiliation</u>	<u>Title</u>
<i>Disease Biology Advisors</i>		
Abul K. Abbas, M.D.	University of California, San Francisco	Professor and Chair, Department of Pathology
John D. Brunzell, M.D.	University of Washington	Professor of Medicine, Division of Metabolism, Endocrinology & Nutrition
Roger D. Cone, Ph.D.	Vollum Institute for Advanced Biomedical Research	Senior Scientist
Neal G. Copeland, Ph.D.	National Cancer Institute	Director, Mouse Cancer Genetics Program
Kenneth H. Gabbay, M.D.	Baylor College of Medicine	Professor of Pediatrics and Molecular & Cell Biology, Head, Section of Molecular Diabetes and Metabolism, Department of Pediatrics
John M. Harlan, M.D.	University of Washington	Professor and Head, Division of Hematology Medicine
Nancy A. Jenkins, Ph.D.	National Cancer Institute	Senior Investigator, Mouse Cancer Genetics Program
Jeffrey L. Noebels, M.D., Ph.D.	Baylor College of Medicine	Professor of Neurology, Neuroscience and Molecular Genetics
Howard A. Rockman, M.D.	Duke University Medical Center	Associate Professor of Medicine
Oliver Smithies, Ph.D.	University of North Carolina	Excellence Professor, Department of Pathology and Laboratory Medicine
Laurence H. Tecott, M.D., Ph.D.	University of California, San Francisco	Associate Professor, Department of Psychiatry
<i>Medicinal Chemistry Advisors</i>		
Ronald T. Borchardt, Ph.D.	University of Kansas	Professor and Chairman, Department of Pharmaceutical Chemistry
Alan R. Katritsky, Ph.D.	University of Florida	Professor of Chemistry
David W. C. MacMillan, Ph.D.	California Institute of Technology	Associate Professor of Chemistry
Nikola Pavletich, Ph.D.	Memorial Sloan-Kettering Cancer Center	Head, Structural Biology of Oncogenes and Tumor Suppressors Laboratory, Howard Hughes Medical Institute Investigator
<i>Chairman, Medical Advisory Board</i>		
Alan S. Nies, M.D.		Former Senior Vice President, Clinical Sciences, Merck & Co., Inc.

## Risk Factors

Our business is subject to risks and uncertainties, including those described below:

### *Risks Related to Our Business*

*We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability*

We have incurred net losses since our inception, including net losses of \$59.7 million for the year ended December 31, 2002. As of December 31, 2002, we had an accumulated deficit of \$149.7 million. We are unsure when we will become profitable, if ever. The size of our net losses will depend, in part, on the rate of growth, if any, in our revenues and on the level of our expenses.

We derive substantially all of our revenues from subscriptions to our LexVision and OmniBank databases, drug discovery alliances, functional genomics collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales, and will continue to do so for the foreseeable future. Our future revenues from database subscriptions, collaborations and alliances are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration. Our future revenues from technology licenses are uncertain because they depend, in large part, on securing new agreements. Subject to limited exceptions, we do not intend to continue to make our compound libraries available for purchase in the future. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future subscribers, collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues.

A large portion of our expenses are fixed, including expenses related to facilities, equipment and personnel. In addition, we expect to spend significant amounts to fund research and development and to enhance our core technologies. As a result, we expect that our operating expenses will continue to increase significantly in the near term and, consequently, we will need to generate significant additional revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

*Our quarterly operating results have been and likely will continue to fluctuate, and we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance*

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including:

- our ability to establish new database subscriptions, research collaborations and technology licenses, and the timing of such arrangements;
- the expiration or other termination of database subscriptions and research collaborations with our collaborators, which may not be renewed or replaced;
- the success rate of our discovery efforts leading to opportunities for new research collaborations and licenses, as well as milestone payments and royalties;
- the timing and willingness of our collaborators to commercialize pharmaceutical products that would result in milestone payments and royalties; and
- general and industry-specific economic conditions, which may affect our and our collaborators' research and development expenditures.

Because of these and other factors, including the risks and uncertainties described in this section, our quarterly operating results have fluctuated in the past and are likely to do so in the future. Due to the likelihood of

fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance. Our operating results in some quarters may not meet the expectations of stock market analysts and investors, which could result in a decline in our stock price.

*We will need additional capital in the future and, if it is not available, we will have to curtail or cease operations*

Our future capital requirements will be substantial and will depend on many factors, including our ability to obtain database subscription, alliance, collaboration and technology license agreements, the amount and timing of payments under such agreements, the level and timing of our research and development expenditures, market acceptance of our products, the resources we devote to developing and supporting our products and other factors. Our capital requirements will increase substantially to the extent we advance potential therapeutics into preclinical and clinical development. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary technologies and businesses.

We anticipate that our existing capital resources and revenues we expect to derive from subscriptions to our databases, drug discovery alliances, functional genomics collaborations and technology licenses will enable us to maintain our currently planned operations at least through the next 12 months. However, we may generate less revenues than we expect, and changes may occur that would consume available capital resources more rapidly than we expect. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds to continue the development of our technologies and complete the commercialization of products, if any, resulting from our technologies. We may be unable to raise sufficient additional capital; if so, we will have to curtail or cease operations.

*We are an early-stage company with an unproven business strategy*

Our business strategy of using our technology platform and, specifically, the discovery of the functions of genes using knockout mice to select promising drug targets and of developing and commercializing our discoveries through collaborations and alliances is unproven. Our success will depend upon our ability to enter into additional collaboration and alliance agreements on favorable terms, determine which genes have potential value as drug targets, discover potential therapeutics for drug targets we consider to have pharmaceutical value, successfully develop such potential therapeutics and select an appropriate commercialization strategy for each potential therapeutic we choose to pursue.

Biotechnology and pharmaceutical companies have successfully developed and commercialized only a limited number of genomics-derived pharmaceutical products to date. We have not proven our ability to identify genomics-derived therapeutics or drug targets with commercial potential, or to develop or commercialize therapeutics or drug targets that we do identify. It is difficult to successfully select those drug targets with the most potential for commercial development and to identify potential therapeutics, and we do not know that any pharmaceutical products based on our drug target discoveries can be successfully commercialized. In addition, we may experience unforeseen technical complications in the processes we use to generate gene knockout mice, conduct *in vivo* analyses, generate compound libraries, develop screening assays for drug targets or conduct screening of compounds against those drug targets. These complications could materially delay or limit the use of those resources, substantially increase the anticipated cost of generating them or prevent us from implementing our processes at appropriate quality and throughput levels.

*We face substantial competition in the discovery of the DNA sequences of genes and their functions and in our drug discovery and product development efforts*

There are a finite number of genes in the human genome, and we believe that the majority of such genes have been identified by us or others conducting genomic research and that virtually all will be identified within the next few years. We face significant competition in our efforts to discover and patent the sequence and other information derived from such genes from entities using alternative, and in some cases higher volume and larger scale, approaches for the same purpose.

We also face competition from other companies in our efforts to discover the functions of genes. Many of these competitors have substantially greater financial, scientific and human resources than we do. A large number of universities and other not-for-profit institutions, many of which are funded by the U.S. and foreign governments, are also conducting research to discover the functions of genes. Competitors could discover and establish patents in genes or gene products that we identify as promising drug targets.

Our ability to use our patent rights to prevent competition in the creation and use of knockout mice outside of the United States is limited. Furthermore, other methods for conducting functional genomics research may ultimately prove superior, in some or all respects, to the use of knockout mice. In addition, technologies more advanced than or superior to our gene targeting and gene trapping technologies may be developed, thereby rendering those technologies obsolete.

We face significant competition from other companies, as well as from universities and other not-for-profit institutions, in our drug discovery and product development efforts. Many of these competitors have substantially greater financial, scientific and human resources than we do. These competitors may develop products earlier than we do, obtain regulatory approvals faster than we can and develop products that are more effective than ours.

*We rely heavily on collaborators to develop and commercialize pharmaceutical products based on genes that we identify as promising candidates for development as drug targets*

Since we do not currently possess the resources necessary to develop, obtain approvals for or commercialize potential pharmaceutical products based on genes contained in our databases or genes that we identify as promising candidates for development as drug targets or therapeutic proteins, we must enter into collaborative arrangements to develop and commercialize these products. We will have limited or no control over the resources that any collaborator may devote to this effort. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct product discovery, development or commercialization activities successfully or in a timely manner. Further, our collaborators may elect not to develop pharmaceutical products arising out of our collaborative arrangements or may not devote sufficient resources to the development, approval, manufacture, marketing or sale of these products. If any of these events occurs, we may not be able to develop or commercialize potential pharmaceutical products.

Some of our agreements provide us with rights to participate in the commercial development of pharmaceutical products derived from our collaborations or access to our databases, technology or intellectual property. We may not be able to obtain such rights in future collaborations or agreements. Our ability to obtain such rights depends in part on the validity of our intellectual property, the advantages and novelty of our technologies and databases and our negotiating position relative to each potential collaborator or customer. Previous attempts by others in the industry to obtain these rights with respect to the development of knockout mice and related technologies have generated considerable controversy, especially in the academic community.

*Any cancellation by or conflicts with our collaborators could harm our business*

Our alliance and collaboration agreements may not be renewed and may be terminated in the event either party fails to fulfill its obligations under these agreements. Any failure to renew or cancellation by a collaborator could mean a significant loss of revenues and volatility in our earnings.

In addition, we may pursue opportunities in fields that could conflict with those of our collaborators. Moreover, disagreements could arise with our collaborators over rights to our intellectual property or our rights to share in any of the future revenues of compounds or therapeutic approaches developed by our collaborators. These kinds of disagreements could result in costly and time-consuming litigation. Any conflict with our collaborators could reduce our ability to obtain future collaboration agreements and could have a negative impact on our relationship with existing collaborators, adversely affecting our business and revenues. Some of our collaborators are also potential competitors or may become competitors in the future. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Any of these developments could harm our product development efforts.



*We have no experience in developing and commercializing pharmaceutical products on our own*

Our ability to develop and commercialize pharmaceutical products on our own will depend on our ability to internally develop preclinical, clinical, regulatory and sales and marketing capabilities, or enter into arrangements with third parties to provide those functions. We may not be successful in developing these capabilities or entering into agreements with third parties on favorable terms, or at all. Further, our reliance upon third parties for these capabilities could reduce our control over such activities and could make us dependent upon these parties. Our inability to develop or contract for these capabilities would significantly impair our ability to develop and commercialize pharmaceutical products.

*We lack the capability to manufacture compounds for preclinical studies and clinical trials and will rely on third parties to manufacture our potential products*

We currently do not have the manufacturing capabilities or experience necessary to produce materials for preclinical studies or clinical trials and intend to rely on collaborators and third-party contractors to produce such materials. We will rely on selected manufacturers to deliver materials on a timely basis and to comply with applicable regulatory requirements, including the FDA's current Good Manufacturing Practices, or GMP. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. If we are unable to contract for production of sufficient quantity and quality of materials on acceptable terms, our product development efforts may be delayed.

*We may engage in future acquisitions, which may be expensive and time consuming and from which we may not realize anticipated benefits*

We may acquire additional businesses, technologies and products, if we determine that these businesses, technologies and products complement our existing technology or otherwise serve our strategic goals. We currently have no commitments or agreements with respect to any acquisitions. If we do undertake any transactions of this sort, the process of integrating an acquired business, technology or product may result in operating difficulties and expenditures and may absorb significant management attention that would otherwise be available for ongoing development of our business. Moreover, we may never realize the anticipated benefits of any acquisition. Future acquisitions could result in potentially dilutive issuances of our equity securities, the incurrence of debt and contingent liabilities and amortization expenses related to intangible assets, which could adversely affect our results of operations and financial condition.

*If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to pursue collaborations or develop our own products*

We are highly dependent on Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, as well as other principal members of our management and scientific staff. The loss of any of these personnel would have a material adverse effect on our business, financial condition or results of operations and could inhibit our product development and commercialization efforts. Although we have entered into employment agreements with some of our key personnel, including Dr. Sands, these employment agreements are for a limited period of time and not all key personnel have employment agreements.

Recruiting and retaining qualified scientific personnel to perform future research and development work will be critical to our success. Competition for experienced scientists is high. Failure to recruit and retain scientific personnel on acceptable terms could prevent us from achieving our business objectives.

*We may encounter difficulties in managing our growth, which could increase our losses*

We have experienced a period of rapid growth that has placed and, if this growth continues, will continue to place a strain on our human and capital resources. If we are unable to manage our growth effectively, our losses could increase. The number of our employees increased from 93 at December 31, 1998 to 122 at December 31, 1999, 287 at December 31, 2000, 484 at December 31, 2001, 572 at December 31, 2002 and 579 at March 3, 2003. Our ability to manage our operations and growth effectively requires us to continue to expend funds to improve our

operational, financial and management controls, reporting systems and procedures. If we are unable to successfully implement improvements to our management information and control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, our management may not have adequate information to manage our day-to-day operations.

*Because all of our functional genomics operations are located at a single facility, the occurrence of a disaster could significantly disrupt our business*

Our OmniBank mouse clone library and its back-up are stored in liquid nitrogen freezers located at our facility in The Woodlands, Texas, and our knockout mouse research operations are carried out entirely at the same facility. While we have developed redundant and emergency backup systems to protect these resources and the facilities in which they are stored, they may be insufficient in the event of a severe fire, flood, hurricane, tornado or similar disaster. If such a disaster significantly damages or destroys the facility in which these resources are maintained, our business could be disrupted until we could regenerate the affected resources and, as a result, our stock price could decline. Our business interruption insurance may not be sufficient to compensate us in the event of a major interruption due to such a disaster.

#### *Risks Related to Our Industry*

*Our ability to patent our discoveries is uncertain because patent laws and their interpretation are highly uncertain and subject to change*

The patent positions of biotechnology firms generally are highly uncertain and involve complex legal and factual questions that will determine who has the right to develop a particular product. No clear policy has emerged regarding the breadth of claims covered in biotechnology patents. The biotechnology patent situation outside the United States is even more uncertain and is currently undergoing review and revision in many countries. Changes in, or different interpretations of, patent laws in the United States and other countries might allow others to use our discoveries or to develop and commercialize our products without any compensation to us. We anticipate that these uncertainties will continue for a significant period of time.

*Our patent applications may not result in enforceable patent rights*

Our disclosures in our patent applications may not be sufficient to meet the statutory requirements for patentability. Our ability to obtain patent protection based on genes or gene sequences will depend, in part, upon identification of a function for the gene or gene sequences sufficient to meet the statutory requirement that an invention have utility and that a patent application describe the invention with sufficient specificity. While the U.S. Patent and Trademark Office has issued guidelines for the examination of patent applications claiming gene sequences, their therapeutic uses and novel proteins encoded by such genes, the impact of these guidelines is uncertain and may delay or negatively affect our patent position. Furthermore, biologic data in addition to that obtained by our current technologies may be required for issuance of patents on human therapeutics. If required, obtaining such biologic data could delay, add substantial costs to, or affect our ability to obtain patent protection. There can be no assurance that the disclosures in our current or future patent applications, including those we may file with our collaborators, will be sufficient to meet these requirements. Even if patents are issued, there may be current or future uncertainty as to the scope of the coverage or protection provided by any such patents.

Other companies or institutions have filed and will file patent applications that attempt to patent genes or gene sequences that may be similar to our patent applications. The U.S. Patent and Trademark Office could decide competing patent claims in an interference proceeding. Any such proceeding would be costly, and we may not prevail. In addition, patent applications filed by third parties may have priority over patent applications we file. In this event, the prevailing party may require us or our collaborators to stop pursuing a potential product or to negotiate a license arrangement to pursue the potential product. We may not be able to obtain a license from the prevailing party on acceptable terms, or at all. In addition, the Human Genome Project, as well as many companies and institutions, have identified genes and deposited partial gene sequences in public databases and are continuing to do so. These public disclosures might limit the scope of our claims or make unpatentable subsequent patent applications on full-length genes.

Some court decisions indicate that disclosure of a partial sequence may not be sufficient to support the patentability of a full-length sequence. These decisions have been confirmed by recent pronouncements of the U.S. Patent and Trademark Office. We believe that these court decisions and the uncertain position of the U.S. Patent and Trademark Office present a significant risk that the U.S. Patent and Trademark Office will not issue patents based on patent disclosures limited to partial gene sequences, like those represented in our human gene trap database. In addition, we are uncertain about the scope of the coverage, enforceability and commercial protection provided by any patents issued primarily on the basis of gene sequence information.

*If other companies and institutions obtain patents claiming the functional uses of genes and gene products based upon gene sequence information and predictions of gene function, we may be unable to obtain patents for our discoveries of biological functions in knockout mice*

We intend to pursue patent protection covering the functions and pharmaceutical utility that we discover for both new and known genes and proteins. While an actual description of the biological function of a gene or protein should enhance a patent position, we cannot assure you that such information will increase the probability of issuance of any patents. Further, many other entities are currently filing patents on genes which are identical or similar to our filings. Many such applications seek to protect partial human gene sequences, full-length gene sequences and the deduced protein products encoded by the sequences while others use biological or other laboratory data. Some of these applications attempt to assign biologic function to the DNA sequences based on computer predictions or patterns of gene expression. There is the significant possibility that patents claiming the functional uses of genes and gene products will be issued to our competitors based on such information.

*We may be involved in patent litigation and other disputes regarding intellectual property rights, and can give no assurances that we will prevail in any such litigation or other dispute*

Our potential products and those of our collaborators may give rise to claims that they infringe the patents of others. This risk will increase as the biotechnology industry expands and as other companies obtain more patents covering the sequences, functions and uses of genes and the drug targets they encode. In addition, many companies have well-established patent portfolios directed to common techniques, methods and means of developing, producing and manufacturing pharmaceutical products. Other companies or institutions could bring legal actions against us or our collaborators for damages or to stop us or our collaborators from manufacturing and marketing the affected products. If any of these actions are successful, in addition to our potential liability for damages, these entities may require us or our collaborators to obtain a license in order to continue to manufacture or market the affected products or may force us to terminate manufacturing or marketing efforts.

We may need to pursue litigation against others to enforce our patents and intellectual property rights. Patent litigation is expensive and requires substantial amounts of management attention. In addition, the eventual outcome of any such litigation is uncertain.

We believe that there will continue to be significant litigation in our industry regarding patent and other intellectual property rights. We have and many of our competitors have and are continuing to expend significant amounts of time, money and management resources on intellectual property litigation. If we become involved in future intellectual property litigation, it could consume a substantial portion of our resources and could negatively affect our results of operations.

Patent litigation involves substantial risks. Each time we sue for patent infringement we face the risk that the patent will be held invalid or unenforceable. Such a determination is binding on us for all future litigation involving that patent. Furthermore, in light of recent U.S. Supreme Court precedent, our ability to enforce our patents against state agencies, including state sponsored universities and research labs, is limited by the Eleventh Amendment to the U.S. Constitution. Finally, opposition by academicians and the government may hamper our ability to enforce our patent against academic or government research laboratories. Enforcement of our patents may cause our reputation in the academic community to be injured.

*Issued patents may not fully protect our discoveries, and our competitors may be able to commercialize products similar to those covered by our issued patents*

Issued patents may not provide commercially meaningful protection against competitors. Other companies or institutions may challenge our or our collaborators' patents or independently develop similar products that could result in an interference proceeding in the Patent and Trademark Office or a legal action. In the event any single researcher or institution infringes upon our or our collaborators' patent rights, enforcing these rights may be difficult and time consuming. Others may be able to design around these patents or develop unique products providing effects similar to our products. We may be required to choose between pursuing litigation against infringers and being unable to recover damages or otherwise enforce our patent rights.

In addition, others may discover uses for genes or proteins other than those uses covered in our patents, and these other uses may be separately patentable. Even if we have a patent claim on a particular gene, the holder of a patent covering the use of that gene could exclude us from selling a product that is based on the same use of that gene. In addition, with respect to certain of our patentable inventions, we have decided not to pursue patent protection outside the United States, both because we do not believe it is cost-effective and because of confidentiality concerns. Accordingly, our international competitors could develop, and receive foreign patent protection for gene sequences and functions for which we are seeking U.S. patent protection.

*Our rights to the use of technologies licensed by third parties are not within our control*

We rely, in part, on licenses to use certain technologies that are material to our business. We do not own the patents that underlie these licenses. Our rights to use these technologies and practice the inventions claimed in the licensed patents are subject to our licensors abiding by the terms of those licenses and not terminating them. In many cases, we do not control the prosecution or filing of the patents to which we hold licenses and rely upon our licensors to prevent infringement of those patents. The scope of our rights under our licenses may be subject to dispute by our licensors or third parties.

*We may be unable to protect our trade secrets*

While we have entered into confidentiality agreements with employees and collaborators, we may not be able to prevent the disclosure of our trade secrets. In addition, other companies or institutions may independently develop substantially equivalent information and techniques.

*We and our collaborators are subject to extensive and uncertain government regulatory requirements, which could increase our operating costs or adversely affect our ability to obtain government approval of products based on genes that we identify in a timely manner or at all*

Drugs and diagnostic products are subject to an extensive and uncertain regulatory approval process by the FDA and comparable agencies in other countries. The regulation of new products is extensive, and the required process of laboratory testing and human studies is lengthy and expensive. The burden of these regulations will fall on us to the extent we develop proprietary products on our own. If the products are the result of a collaboration effort, these burdens may fall on our collaborating partner or may be shared with us. We may not be able to obtain FDA approvals for those products in a timely manner, or at all. We may encounter significant delays or excessive costs in our efforts to secure necessary approvals or licenses. Even if we obtain FDA regulatory approvals, the FDA extensively regulates manufacturing, labeling, distributing, marketing, promotion and advertising after product approval. Moreover, several of our product development areas may involve relatively new technology and have not been the subject of extensive product testing in humans. The regulatory requirements governing these products and related clinical procedures remain uncertain and the products themselves may be subject to substantial review by foreign governmental regulatory authorities that could prevent or delay approval in those countries. Regulatory requirements ultimately imposed on our products could limit our ability to test, manufacture and, ultimately, commercialize our products.

Since we develop animals containing changes in their genetic make-up, we may become subject to a variety of laws, guidelines, regulations and treaties specifically directed at genetically modified organisms, or GMOs. The area of environmental releases of GMOs is rapidly evolving and is currently subject to intense regulatory scrutiny,

particularly internationally. If we become subject to these laws we could incur substantial compliance costs. For example, the Biosafety Protocol, or the BSP, a recently adopted treaty, is expected to cover certain shipments from the United States to countries abroad that have signed the BSP. The BSP is also expected to cover the importation of living modified organisms, a category that could include our animals. If our animals are not contained as described in the BSP, our animals could be subject to the potentially extensive import requirements of countries that are signatories to the BSP.

*The uncertainty of pharmaceutical pricing and reimbursement may decrease the commercial potential of our products and affect our ability to raise capital*

Our ability and the ability of our collaborators to successfully commercialize pharmaceutical products may depend in part on the extent to which reimbursement for the cost of such products and related treatment will be available from government health administration authorities, private health coverage insurers and other organizations. The pricing, availability of distribution channels and reimbursement status of newly approved pharmaceutical products is highly uncertain. As a result, adequate third-party coverage may not be available for us to maintain price levels sufficient for realization of an appropriate return on our investment in product discovery and development.

In certain foreign markets, pricing or profitability of healthcare products is subject to government control. In the U.S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control. In addition, an increasing emphasis on managed care in the U.S. has and will continue to increase the pressure on pharmaceutical pricing. While we cannot predict the adoption of any such legislative or regulatory proposals or the effect such proposals or managed care efforts may have on our business, the announcement of such proposals or efforts could harm our ability to raise capital, and the adoption of such proposals or efforts could harm our results of operations. Further, to the extent that such proposals or efforts harm other pharmaceutical companies that are our prospective collaborators, this may reduce our ability to establish corporate collaborations. In addition, third-party payers are increasingly challenging the prices charged for medical products and services. We do not know whether consumers, third-party payers and others will consider any products that we or our collaborators develop to be cost effective or that reimbursement to the consumer will be available or will be sufficient to allow us or our collaborators to sell such products on a competitive basis.

*Security risks in electronic commerce or unfavorable Internet regulation may deter future use of our products and services*

We provide access to our databases and the opportunity to acquire our knockout mice on the Internet. A fundamental requirement to conduct Internet-based electronic commerce is the secure transmission of confidential information over public networks. Advances in computer capabilities, new discoveries in the field of cryptography or other developments may result in a compromise or breach of the algorithms we use to protect proprietary information in our OmniBank database. Anyone who is able to circumvent our security measures could misappropriate our proprietary information, confidential customer information or cause interruptions in our operations. We may be required to incur significant costs to protect against security breaches or to alleviate problems caused by breaches. Further, a well-publicized compromise of security could deter people from using the Internet to conduct transactions that involve transmitting confidential information.

Because of the growth in electronic commerce, Congress has held hearings on whether to regulate providers of services and transactions in the electronic commerce market, and federal or state authorities could enact laws, rules or regulations affecting our business or operations. If enacted and applied to our business, these laws, rules or regulations could render our business or operations more costly, burdensome, less efficient or impracticable.

*We use hazardous chemicals and radioactive and biological materials in our business; any disputes relating to improper handling, storage or disposal of these materials could be time consuming and costly*

Our research and development processes involve the use of hazardous materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge or any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be

subject to civil damages in the event of an improper or unauthorized release of, or exposure of individuals to, these hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development or production efforts.

*We may be sued for product liability*

We or our collaborators may be held liable if any product we or our collaborators develop, or any product which is made with the use or incorporation of any of our technologies, causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Although we currently have and intend to maintain product liability insurance, this insurance may become prohibitively expensive, or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products developed by us or our collaborators. If we are sued for any injury caused by our or our collaborators' products, our liability could exceed our total assets.

*Public perception of ethical and social issues may limit or discourage the use of our technologies, which could reduce our revenues*

Our success will depend in part upon our ability to develop products discovered through our knockout mouse technologies. Governmental authorities could, for ethical, social or other purposes, limit the use of genetic processes or prohibit the practice of our knockout mouse technologies. Claims that genetically engineered products are unsafe for consumption or pose a danger to the environment may influence public perceptions. The subject of genetically modified organisms, like knockout mice, has received negative publicity and aroused public debate in some countries. Ethical and other concerns about our technologies, particularly the use of genes from nature for commercial purposes and the products resulting from this use, could adversely affect the market acceptance of our technologies.

*Item 2. Properties*

We currently lease approximately 300,000 square feet of space for our corporate offices and laboratories in buildings located in The Woodlands, Texas, a suburb of Houston, Texas, and approximately 118,000 square feet of space for offices and laboratories near Princeton, New Jersey.

Our facilities in The Woodlands, Texas include two state-of-the art animal facilities totaling approximately 100,000 square feet. These facilities, completed in 1999 and 2002, respectively, were custom designed for the generation and analysis of knockout mice and are accredited by AAALAC International (Association for Assessment and Accreditation of Laboratory Animal Care). These facilities enable us to maintain in-house control over our entire *in vivo* validation process, from the generation of ES cell clones through the completion of *in vivo* analysis, in a specific pathogen free (SPF) environment. We believe these facilities, which are among the largest and most sophisticated of their kind in the world, provide us with significant strategic and operational advantages relative to our competitors.

In October 2000, we entered into a synthetic lease agreement under which the lessor purchased our existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility. Including the purchase price for our existing facilities, the synthetic lease, as amended, provides for funding of up to \$55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.4%, our total lease payments for our existing facilities and the new facilities would be approximately \$0.9 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or we may purchase the properties for a price equal to the \$55.0 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If we

elect not to renew the lease or purchase the properties, we may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If we elect to arrange for the sale of the properties or surrender the properties to the lessor, we have guaranteed approximately 86% of the total original cost as the residual fair value of the properties.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a ten-year lease for a 76,000 square-foot facility in Hopewell, New Jersey. The lease provides for an escalating yearly rent payment of \$1.3 million in the first year, \$1.7 million in years two and three, \$1.8 million in years four to six, \$2.0 million in years seven to nine and \$2.1 million in year ten. The lease also provides our subsidiary with the option in the second year of the lease to borrow \$2.0 million in tenant improvement funds from the landlord, at which time rental payments due under the lease will increase as the tenant improvement allowance is amortized over a ten-year period. We are the guarantor of the obligations of our subsidiary under the lease. We also lease space in East Windsor, New Jersey under an agreement that expires in January 2004. Our aggregate rent expense under the New Jersey leases is approximately \$2.5 million per year.

We believe that our facilities are well-maintained, in good operating condition and acceptable for our current operations.

**Item 3. *Legal Proceedings***

We are not presently a party to any material legal proceedings.

**Item 4. *Submission of Matters to a Vote of Security Holders***

No matters were submitted during the fourth quarter of the year ended December 31, 2002.

## PART II

### Item 5. *Market for Registrant's Common Equity and Related Stockholder Matters*

Our common stock has been quoted on The Nasdaq National Market under the symbol "LEXG" since April 7, 2000. Prior to that time, there was no public market for our common stock. The following table sets forth, for the periods indicated, the range of the high and low closing prices per share for our common stock as reported on The Nasdaq National Market.

	High	Low
<b>2001</b>		
First Quarter.....	\$ 15.00	\$ 6.56
Second Quarter .....	\$ 12.50	\$ 5.69
Third Quarter .....	\$ 12.75	\$ 5.87
Fourth Quarter .....	\$ 11.90	\$ 7.25
<b>2002</b>		
First Quarter.....	\$ 12.04	\$ 7.98
Second Quarter .....	\$ 9.00	\$ 4.12
Third Quarter .....	\$ 6.18	\$ 3.51
Fourth Quarter .....	\$ 5.25	\$ 3.35

As of March 10, 2003, there were approximately 253 holders of record of our common stock.

We have never paid cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future.



## Item 6. Selected Financial Data

The statement of operations data for the year ended December 31, 2002 and the balance sheet data as of December 31, 2002 have been derived from our audited financial statements included elsewhere in this annual report on Form 10-K that have been audited by Ernst & Young LLP, independent auditors. The statements of operations data for each of the years ended December 31, 2001 and 2000, and the balance sheet data as of December 31, 2001, have been derived from our audited financial statements included elsewhere in this annual report on Form 10-K that have been audited by Arthur Andersen LLP, independent public accountants who have ceased operations. The statements of operations data for the years ended December 31, 1999 and 1998, and the balance sheet data as of December 31, 2000, 1999 and 1998 have been derived from our audited financial statements not included in this annual report on Form 10-K. Our historical results are not necessarily indicative of results to be expected for any future period. The data presented below have been derived from financial statements that have been prepared in accordance with accounting principles generally accepted in the United States and should be read with our financial statements, including the notes, and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this annual report on Form 10-K.

	Year Ended December 31,				
	2002	2001	2000	1999	1998
(in thousands, except per share data)					
<b>Statements of Operations Data:</b>					
Revenues .....	\$ 35,200	\$ 30,577	\$ 14,459	\$ 4,738	\$ 2,242
Operating expenses:					
Research and development, including stock-based compensation of \$5,155 in 2002, \$5,539 in 2001 and \$10,883 in 2000 .....	74,859	53,355	31,647	14,646	8,410
General and administrative, including stock-based compensation of \$5,113 in 2002, \$5,231 in 2001 and \$9,958 in 2000 .....	23,234	20,861	18,289	2,913	2,024
Total operating expenses .....	98,093	74,216	49,936	17,559	10,434
Loss from operations .....	(62,893)	(43,639)	(35,477)	(12,821)	(8,192)
Interest and other income, net .....	3,223	8,467	9,483	346	711
Net loss .....	(59,670)	(35,172)	(25,994)	(12,475)	(7,481)
Accretion on redeemable convertible preferred stock ..	—	—	(134)	(536)	(357)
Net loss attributable to common stockholders .....	\$ (59,670)	\$ (35,172)	\$ (26,128)	\$ (13,011)	\$ (7,838)
Net loss per common share, basic and diluted .....	\$ (1.14)	\$ (0.70)	\$ (0.63)	\$ (0.53)	\$ (0.32)
Shares used in computing net loss per common share, basic and diluted .....	52,263	50,213	41,618	24,530	24,445

	As of December 31,				
	2002	2001	2000	1999	1998
(in thousands)					
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and investments, including restricted cash and investments of \$57,710 in 2002 \$43,338 in 2001 and \$13,879 in 2000 .....	\$ 123,096	\$ 166,840	\$ 202,680	\$ 9,156	\$ 19,422
Working capital .....	111,833	147,663	194,801	2,021	18,102
Total assets .....	201,772	239,990	220,693	22,295	28,516
Long-term debt, net of current portion .....	4,000	—	1,834	3,577	5,024
Redeemable convertible preferred stock .....	—	—	—	30,050	29,515
Accumulated deficit .....	(149,745)	(90,075)	(54,903)	(28,909)	(16,434)
Stockholders' equity (deficit) .....	169,902	218,372	207,628	(21,937)	(9,035)

## Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations*

The following discussion and analysis should be read with "Selected Financial Data" and our financial statements and notes included elsewhere in this annual report on Form 10-K.

### Overview

We are a biopharmaceutical company focused on the discovery of breakthrough treatments for human disease. We are using gene knockout technology to systematically discover the physiological functions of genes in living mammals, or *in vivo*. We generate our gene function discoveries using knockout mice – mice whose DNA has been altered to disrupt, or "knock out," the function of the altered gene. Our patented gene trapping and gene targeting technologies enable us to rapidly generate these knockout mice by altering the DNA of genes in a special variety of mouse cells, called embryonic stem (ES) cells, which can be cloned and used to generate mice with the altered gene. We employ an integrated platform of advanced medical technologies to systematically discover and validate which genes, when knocked out, result in a favorable medical profile with pharmaceutical utility. We then pursue those genes and the proteins they encode as potential targets for therapeutic intervention in our drug discovery programs.

We employ internal resources and drug discovery alliances to discover potential small molecule drugs, therapeutic antibodies and therapeutic proteins for *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We use our own sophisticated libraries of drug-like chemical compounds and an industrialized medicinal chemistry platform to identify small molecule drug candidates for our *in vivo*-validated drug targets. We have established alliances with Genentech, Inc. for the discovery of therapeutic proteins and antibody targets; with Abgenix, Inc. for the discovery and development of therapeutic antibodies based on our drug target discoveries; and with Incyte Genomics, Inc. for the discovery and development of therapeutic proteins. In addition, we have established collaborations and license agreements with many other leading pharmaceutical and biotechnology companies under which we receive fees and, in many cases, are eligible to receive milestone and royalty payments, for access to some of our technologies and discoveries for use in their own drug discovery efforts.

We derive substantially all of our revenues from subscriptions to our databases, drug discovery alliances, functional genomics collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales. To date, we have generated a substantial portion of our revenues from a limited number of sources.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including our success in establishing research collaborations, technology licenses and new database subscriptions, expirations of our research collaborations and database subscriptions, the success rate of our discovery efforts leading to opportunities for new research collaborations and licenses, as well as milestone payments and royalties, the timing and willingness of collaborators to commercialize products which may result in royalties, and general and industry-specific economic conditions which may affect research and development expenditures. Our future revenues from database subscriptions, collaborations and alliances are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration. Our future revenues from technology licenses are uncertain because they depend, in large part, on securing new agreements. Subject to limited exceptions, we do not intend to continue to make our compound libraries available for purchase in the future. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future subscribers, collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues. Because of these and other factors, our quarterly operating results have fluctuated in the past and are likely to do so in the future, and we do not believe that quarter-to-quarter comparisons of our operating results are a good indication of our future performance.

Since our inception, we have incurred significant losses and, as of December 31, 2002, we had an accumulated deficit of \$149.7 million. Our losses have resulted principally from costs incurred in research and development, general and administrative costs associated with our operations, and non-cash stock-based compensation expenses associated with stock options granted to employees and consultants prior to our April 2000 initial public offering. Research and development expenses consist primarily of salaries and related personnel costs,

material costs, facility costs, depreciation on property and equipment, legal expenses resulting from intellectual property prosecution and other expenses related to our drug discovery and LexVision programs, the development and analysis of knockout mice and our other functional genomics research efforts, and the development of compound libraries. General and administrative expenses consist primarily of salaries and related expenses for executive, finance and other administrative personnel, professional fees and other corporate expenses including business development and general legal activities, as well as expenses related to our patent infringement litigation against Deltagen, Inc., which was settled in September 2001. In connection with the expansion of our drug discovery programs and our functional genomics research efforts, we expect to incur increasing research and development and general and administrative costs. As a result, we will need to generate significantly higher revenues to achieve profitability.

As of December 31, 2002, we had net operating loss carryforwards of approximately \$114.0 million. We also had research and development tax credit carryforwards of approximately \$7.1 million. The net operating loss and credit carryforwards will expire at various dates beginning in 2011, if not utilized. Utilization of the net operating losses and credits may be significantly limited due to a change in ownership as defined by provisions of the Internal Revenue Code of 1986 and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

### **Critical Accounting Policies**

#### ***Revenue Recognition***

We recognize revenues when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable, and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned.

Fees for access to our databases and other functional genomics resources are recognized ratably over the subscription or access period. Collaborative research payments are recognized as revenue as we perform our obligations related to such research to the extent such fees are non-refundable. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Non-refundable technology license fees are recognized as revenue upon the grant of the license when performance is complete and there is no continuing involvement.

Revenues recognized from multiple element contracts are allocated to each element of the arrangement based on the relative fair value of the elements. The determination of fair value of each element is based on objective evidence. When revenues for an element are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligation associated with the element is completed. When revenues for an element are not specifically tied to a separate earnings process, they are recognized ratably over the term of the agreement.

A change in our revenue recognition policy or changes in the terms of contracts under which we recognize revenues could have an impact on the amount and timing of our recognition of revenues.

#### ***Research and Development Expenses***

Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Patent costs and technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.

#### ***Stock-Based Compensation***

Deferred stock-based compensation and related amortization represents the difference between the exercise price of stock options granted and the fair value of our common stock at the applicable date of grant. Stock-based compensation is amortized as research and development expense or general and administrative expense, as appropriate, over the vesting period of the individual stock options for which it was recorded, generally four years.

If employees and consultants continue to vest in accordance with their individual stock options, we expect to record amortization expense for deferred stock-based compensation of \$10.2 million during 2003 and \$0.9 million during 2004. The amount of stock-based compensation expense to be recorded in future periods may decrease if unvested stock options for which deferred stock-based compensation has been recorded are subsequently canceled or forfeited or may increase if additional stock options are granted to individuals other than employees or directors.

#### *Goodwill Impairment*

Goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if we encounter events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2002.

#### *Recent Accounting Pronouncements*

In November 2002, the Financial Accounting Standards Board, or FASB issued Interpretation, or FIN, No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others." FIN 45 elaborates on the existing disclosure requirements for most guarantees, including residual value guarantees issued in conjunction with operating lease agreements. It also clarifies that at the time a company issues a guarantee, the company must recognize an initial liability for the fair value of the obligation it assumes under that guarantee and must disclose that information in its interim and annual financial statements. The initial recognition and measurement provisions apply on a prospective basis to guarantees issued or modified after December 31, 2002. The disclosure requirements are effective for financial statements of interim or annual periods ending after December 15, 2002. Our adoption of FIN 45 will not have a material impact on our results of operations and financial position.

In November 2002, the Emerging Issues Task Force, or EITF, reached a consensus on EITF Issue No. 00-21, "Accounting for Revenue Arrangements with Multiple Deliverables." This consensus requires that revenue arrangements with multiple deliverables be divided into separate units of accounting if the delivered items have value to the customer on a standalone basis, there is objective and reliable evidence of fair value of the undelivered items and, if the arrangement includes a general right of return, performance of the undelivered item is considered probable and substantially in our control. The final consensus will be applicable to agreements entered into in fiscal periods beginning after June 15, 2003, with early adoption permitted.

In December 2002, the FASB issued Statement of Financial Accounting Standards, or SFAS, No. 148, "Accounting for Stock-Based Compensation – Transition and Disclosure." This statement amends SFAS 123, "Accounting for Stock-Based Compensation," to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amends the disclosure requirements of SFAS 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based accounting for employee compensation and the effect of the method used on reported results. The Company is currently evaluating whether to adopt the fair value based method.

In January 2003, the FASB issued FIN 46, "Consolidation of Variable Interest Entities." FIN 46 requires that unconsolidated variable interest entities be consolidated by their primary beneficiaries. A primary beneficiary is the party that absorbs a majority of the entity's expected losses or residual benefits. FIN 46 applies immediately to variable interest entities created after January 31, 2003 and to existing variable interest entities in the periods beginning after June 15, 2003. We are evaluating whether the adoption of FIN 46 will require us to consolidate the lessor under our synthetic lease. If such consolidation is required, our balance sheet will reflect as assets additional property and equipment approximating the \$55.0 million funded under the synthetic lease for property and improvements, less accumulated depreciation, and a similar amount as a liability. In addition, we will be required to depreciate such improvements over their useful lives. We may, however, elect to restructure or replace the synthetic lease prior to the adoption of FIN 46, whether or not such consolidation would be required. We believe that the

consolidation of the lessor, if required, will not have a material adverse effect on our financial condition or results of operations.

## Results of Operations

### *Years Ended December 31, 2002 and 2001*

**Revenues.** Total revenues increased 15% to \$35.2 million in 2002 from \$30.6 million in 2001. The increase of \$4.6 million was primarily attributable to a \$5.9 million increase in revenues from functional genomics collaborations and our drug discovery alliance with Incyte and a \$3.1 million increase in revenues from database subscription and technology license fees, offset in part by a \$4.4 million decrease in compound libraries and other revenue. We did not make our compound libraries available for purchase in 2002 and, subject to limited exceptions, do not intend to make our compound libraries available for purchase in the future.

In 2002, Incyte, Bristol-Myers Squibb Company and Millennium Pharmaceuticals, Inc. represented 28%, 14% and 11% of revenues, respectively. In 2001, Incyte, Bristol-Myers Squibb and Merck & Co., Inc. represented 16%, 13% and 12% of revenues, respectively.

**Research and Development Expenses.** Research and development expenses increased 40% to \$74.9 million in 2002 from \$53.4 million in 2001. The increase of \$21.5 million was primarily attributable to increased personnel and facility costs to support the expansion of our drug discovery programs, including a full year of medicinal chemistry operations, the development and analysis of knockout mice and our other functional genomics research efforts. Research and development expenses for 2002 and 2001 included \$5.2 million and \$5.5 million, respectively, of stock-based compensation primarily relating to option grants made prior to our April 2000 initial public offering.

**General and Administrative Expenses.** General and administrative expenses increased 11% to \$23.2 million in 2002 from \$20.9 million in 2001. The increase of \$2.3 million was due primarily to additional personnel costs offset by a reduction in legal costs as a result of the September 2001 settlement of our patent infringement litigation against Deltagen, Inc. General and administrative expenses for 2002 and 2001 included \$5.1 million and \$5.2 million, respectively, of stock-based compensation primarily relating to option grants made prior to our April 2000 initial public offering.

**Interest and Other Income.** Interest and other income decreased 63% to \$3.2 million in 2002 from \$8.8 million in 2001. This decrease resulted from lower cash and investment balances and lower average interest rates during 2002.

**Net Loss and Net Loss Per Common Share.** Net loss attributable to common shareholders increased to \$59.7 million in 2002 from \$35.2 million in 2001. Net loss per common share increased to \$1.14 in 2002 from \$0.70 in 2001. Excluding stock-based compensation expense of \$10.3 million and \$10.8 million in 2002 and 2001, respectively, we would have had a net loss of \$49.4 million and net loss per common share of \$0.95 in 2002, as compared to a net loss of \$24.4 million and net loss per common share of \$0.49 in 2001.

### *Years Ended December 31, 2001 and 2000*

**Revenues.** Total revenues increased 111% to \$30.6 million in 2001 from \$14.5 million in 2000. The increase of \$16.1 million was primarily attributable to a \$10.2 million increase in revenues from database subscription and technology license fees, a \$1.7 million increase in revenues from functional genomics collaborations and our drug discovery alliance with Incyte and revenues of \$4.5 million from compound library sales, offset in part by a \$0.3 million decrease in other revenue.

In 2001, Incyte, Bristol-Myers Squibb and Merck represented 16%, 13% and 12% of revenues, respectively. In 2000, the Merck Genome Research Institute and Millennium represented 35% and 14% of revenues, respectively.

*Research and Development Expenses.* Research and development expenses increased 69% to \$53.4 million in 2001 from \$31.6 million in 2000. The increase of \$21.8 million was attributable to continued growth of research and development activities, primarily related to increased personnel costs to support the expansion of our drug discovery programs, the development and analysis of knockout mice and our other functional genomics research efforts, offset in part by lower stock-based compensation in 2001. Research and development expenses for 2001 and 2000 included \$5.5 million and \$10.9 million, respectively, of stock-based compensation primarily relating to option grants made prior to our April 2000 initial public offering.

*General and Administrative Expenses.* General and administrative expenses increased 14% to \$20.9 million in 2001 from \$18.3 million in 2000. The increase of \$2.6 million was due primarily to additional personnel costs for business development and finance and administration, as well as expenses associated with our patent infringement litigation against Deltagen, offset in part by lower stock-based compensation in 2001. General and administrative expenses for 2001 and 2000 included \$5.2 million and \$10.0 million, respectively, of stock-based compensation primarily relating to option grants made prior to our April 2000 initial public offering.

*Interest and Other Income.* Interest income decreased 11% to \$8.8 million in 2001 from \$9.9 million in 2000. This decrease resulted from lower cash and investment balances and lower average interest rates on our investments.

*Net Loss and Net Loss Per Common Share.* Net loss attributable to common stockholders increased to \$35.2 million in 2001 from \$26.1 million in 2000. Net loss per common share increased to \$0.70 in 2001 from \$0.63 in 2000. Excluding stock-based compensation expense of \$10.8 million and \$20.8 million in 2001 and 2000, respectively, and assuming the conversion of the redeemable convertible preferred stock into common stock occurred on the date of original issuance (May 1998), we would have had a net loss of \$24.4 million and net loss per common share of \$0.49 in 2001, as compared to a net loss of \$5.2 million and net loss per common share of \$0.11 in 2000.

#### **Liquidity and Capital Resources**

We have financed our operations from inception primarily through sales of common and preferred stock, contract and milestone payments to us under our database subscription, collaboration and license agreements, equipment financing arrangements and leasing arrangements. From our inception through December 31, 2002, we had received net proceeds of \$242.7 million from issuances of common and preferred stock, including \$203.2 million of net proceeds from the initial public offering of our common stock in April 2000. In addition, from our inception through December 31, 2002, we received \$101.7 million in cash payments from database subscription and technology license fees, drug discovery alliances, functional genomics collaborations, sales of compound libraries and reagents and government grants, of which \$88.5 million had been recognized as revenues through December 31, 2002.

As of December 31, 2002, we had \$123.1 million in cash, cash equivalents and short-term and long-term investments (including \$57.7 million of restricted cash and investments), as compared to \$166.8 million (including \$43.3 million of restricted cash and investments) as of December 31, 2001. We used cash of \$28.8 million in operations in 2002. This consisted primarily of the net loss for the year of \$59.7 million offset by non-cash charges of \$10.3 million related to stock-based compensation expense, \$9.1 million related to depreciation expense and \$1.2 million related to amortization of intangible assets other than goodwill; a \$5.6 million increase in deferred revenue; and changes in other operating assets and liabilities of \$4.5 million. Investing activities provided cash of \$47.2 million in 2002, principally as a result of net maturities of short-term investments and the sale of long-term investments, offset by an increase in restricted cash and purchases of property and equipment. We received cash of \$4.6 million in financing activities in 2002, consisting principally of proceeds from a \$4.0 million loan and stock option exercises.

In October 2000, we entered into a synthetic lease agreement under which the lessor purchased our existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility for the distribution of utilities and related services among our facilities. Including the purchase price for our existing facilities, the

synthetic lease, as amended, provided for funding of up to \$55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.4%, our total lease payments would be approximately \$0.9 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or we may purchase the properties for a price equal to the \$55.0 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If we elect not to renew the lease or purchase the properties, we may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If we elect to arrange for the sale of the properties or surrender the properties to the lessor, we have guaranteed approximately 86% of the total original cost as the residual fair value of the properties. We are required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement. In addition, we have agreed to maintain cash and investments of at least \$12.0 million in excess of our restricted cash and investments. If our cash and investments fall below that level, we may be required to seek a waiver of that agreement or to purchase the properties or arrange for their sale to a third party. Because our cost to purchase the properties would not materially exceed the \$55.0 million funded under the synthetic lease for property and improvements and would likely be less than the amount of restricted cash and investments we are required to maintain under the synthetic lease, we believe that any requirement that we do so would not have a material adverse effect on our financial condition. As of December 31, 2002 and 2001, we maintained restricted cash and investments of \$57.2 million and \$43.3 million, respectively, to collateralize funding for property and improvements under the synthetic lease of \$55.0 million and \$41.7 million.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a ten-year lease for a 76,000 square-foot facility in Hopewell, New Jersey. The lease provides for an escalating yearly rent payment of \$1.3 million in the first year, \$1.7 million in years two and three, \$1.8 million in years four to six, \$2.0 million in years seven to nine and \$2.1 million in year ten. The lease also provides our subsidiary with the option in the second year of the lease to borrow \$2.0 million in tenant improvement funds from the landlord, at which time rental payments due under the lease will increase as the tenant improvement allowance is amortized over a ten-year period. We are the guarantor of the obligations of our subsidiary under the lease.

In December 2002, we borrowed \$4.0 million under a note agreement with Genentech. The proceeds of the loan are to be used to fund research efforts under our alliance with Genentech for the discovery of therapeutic proteins and antibody targets. The note matures on or before December 31, 2005, but we may prepay it at any time. We may repay the note, at our option, in cash, in shares of our common stock valued at the then-current market value, or in a combination of cash and shares, subject to certain limitations. The note accrues interest at an annual rate of 8%, compounded quarterly.

Including the lease and debt obligations described above, we had incurred the following contractual obligations as of December 31, 2002:

Contractual Obligations	Payments due by period (in millions)				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Long-term debt.....	\$ 4.0	—	\$ 4.0	—	—
Capital lease obligations .....	—	—	—	—	—
Operating leases .....	22.7	3.5	5.6	4.7	8.9
Other long-term liabilities reflected on our balance sheet under GAAP .....	0.7	—	—	0.3	0.4
Total .....	<u>\$ 27.4</u>	<u>\$ 3.5</u>	<u>\$ 9.6</u>	<u>\$ 5.0</u>	<u>\$ 9.3</u>

Our future capital requirements will be substantial and will depend on many factors, including our ability to obtain database subscription, alliance, collaboration and technology license agreements, the amount and timing of payments under such agreements, the level and timing of our research and development expenditures, market acceptance of our products, the resources we devote to developing and supporting our products and other factors. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary technologies and businesses. We expect to devote substantial capital resources to continue our research and development efforts, to expand our support and product development

activities, and for other general corporate activities. We believe that our current unrestricted cash and investment balances and revenues we expect to derive from subscriptions to our databases, functional genomics collaborations, technology licenses and drug discovery alliances will be sufficient to fund our operations at least through the next 12 months. During or after this period, if cash generated by operations is insufficient to satisfy our liquidity requirements, we will need to sell additional equity or debt securities, restructure or replace our synthetic lease to reduce the required amount of restricted cash and investments, or obtain additional credit arrangements. Additional financing may not be available on terms acceptable to us or at all. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders.

#### **Disclosure about Market Risk**

We are exposed to limited market and credit risk on our cash equivalents which have maturities of three months or less. We maintain a short-term investment portfolio which consists of U.S. government agency debt obligations, investment grade commercial paper, corporate debt securities and certificates of deposit that mature three to twelve months from the time of purchase, which we believe are subject to limited market and credit risk. We currently do not hedge interest rate exposure or hold any derivative financial instruments in our investment portfolio.

We have operated primarily in the United States and substantially all sales to date have been made in U.S. dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations.

#### **Item 7A. *Quantitative and Qualitative Disclosures About Market Risk***

See "Disclosure about Market Risk" under "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" for quantitative and qualitative disclosures about market risk.

#### **Item 8. *Financial Statements and Supplementary Data***

The financial statements required by this Item are incorporated under Item 15 in Part IV of this report.

#### **Item 9. *Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.***

On March 26, 2002, the Board of Directors and its audit committee dismissed Arthur Andersen LLP as our independent public accountants and engaged Ernst & Young LLP to serve as our independent auditors for the fiscal year ending December 31, 2002, subject to stockholder ratification.

Arthur Andersen's report on our consolidated financial statements for the fiscal year ended December 31, 2001 did not contain an adverse opinion or disclaimer of opinion, nor was it qualified or modified as to uncertainty, audit scope or accounting principles.

During the fiscal year ended December 31, 2001 and through the date of the Board of Directors' decision, there were no disagreements with Arthur Andersen on any matter of accounting principle or practice, financial statement disclosure, or auditing scope or procedure which, if not resolved to Arthur Andersen's satisfaction, would have caused them to make reference to the subject matter in connection with their report on our consolidated financial statements for such year; and there were no reportable events as defined in Item 304(a)(1)(v) of Regulation S-K.

During the fiscal year ended December 31, 2001 and through the date of the Board of Directors' decision, we did not consult Ernst & Young with respect to the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on our consolidated financial statements, or any other matters or reportable events as set forth in Items 304(a)(2)(i) and (ii) of Regulation S-K.



### PART III

#### **Item 10. Directors and Executive Officers of the Registrant**

The information required by this Item as to our directors and executive officers is hereby incorporated by reference from the information appearing under the captions "Election of Directors" and "Executive Officers" in our definitive proxy statement which involves the election of directors and is to be filed with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2002.

#### **Item 11. Executive Compensation**

The information required by this Item as to our management is hereby incorporated by reference from the information appearing under the captions "Executive Compensation" and "Election of Director – Director Compensation" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2002. Notwithstanding the foregoing, in accordance with the instructions to Item 402 of Regulation S-K, the information contained in our proxy statement under the sub-heading "Report of the Compensation Committee of the Board of Directors" and "Performance Graph" shall not be deemed to be filed as part of or incorporated by reference into this annual report on Form 10-K.

#### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this Item as to the ownership by management and others of our securities is hereby incorporated by reference from the information appearing under the caption "Stock Ownership of Certain Beneficial Owners and Management" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2002.

### EQUITY COMPENSATION PLAN INFORMATION

The following table presents aggregate summary information as of December 31, 2002 regarding the common stock that may be issued upon exercise of options, warrants and rights under all of our existing equity compensation plans, including our 2000 Equity Incentive Plan, 2000 Non-Employee Directors' Stock Option Plan and Coelacanth Corporation 1999 Stock Option Plan.

Plan Category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights	(b) Weighted average exercise price per share of outstanding options, warrants and rights	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders (1) .....	11,282,188	\$6.5006	2,124,606 (3)(4)(5)
Equity compensation plans not approved by security holders (2) .....	89,979	2.6807	—
Total .....	11,372,167	\$6.4704	2,124,606

- (1) Consists of shares of our common stock issued or remaining available for issuance under our 2000 Equity Incentive Plan and 2000 Non-Employee Directors' Stock Option Plan.
- (2) Consists of shares of our common stock issuable upon the exercise of options granted under the Coelacanth Corporation 1999 Stock Option Plan, which we assumed in connection with our July 2001 acquisition of Coelacanth Corporation.
- (3) Includes 1,605,106 shares available for future issuance under our 2000 Equity Incentive Plan, some or all of which may be awarded as stock bonuses.

- (4) Our 2000 Equity Incentive Plan provides that on each January 1, the number of shares available for issuance under the plan will be automatically increased by the greater of (i) five percent of our outstanding shares on a fully-diluted basis or (ii) the number of shares that could be issued under awards granted under the plan during the prior year. Our Board of Directors may provide for a lesser increase in the number of shares available for issuance under the plan.
- (5) Our 2000 Non-Employee Directors' Stock Option Plan provides that on the day following each annual meeting of stockholders, the number of shares available for issuance under the plan will be automatically increased by the greater of (i) 0.3% of our outstanding shares on a fully-diluted basis or (ii) the number of shares that could be issued under options granted under the plan during the prior year. Our Board of Directors may provide for a lesser increase in the number of shares available for issuance under the plan.

#### *Coelacanth Corporation 1999 Stock Option Plan*

We assumed the Coelacanth Corporation 1999 Stock Option Plan and the outstanding stock options under the plan in connection with our July 2001 acquisition of Coelacanth. We will not grant any further options under the plan. As outstanding options under the plan expire or terminate, the number of shares authorized for issuance under the plan will be correspondingly reduced.

The purpose of the plan was to provide an opportunity for employees, directors and consultants of Coelacanth to acquire a proprietary interest, or otherwise increase their proprietary interest, in Coelacanth as an incentive to continue their employment or service. Both incentive and nonstatutory options are outstanding under the plan. Most outstanding options vest over time and expire ten years from the date of grant. The exercise price of options awarded under the plan was determined by the plan administrator at the time of grant. In general, incentive stock options have an exercise price of 100% or more of the fair market value of Coelacanth common stock on the date of grant and nonstatutory stock options have an exercise price as low as 85% of fair market value on the date of grant.

#### *Item 13. Certain Relationships and Related Transactions*

The information required by this Item as to certain business relationships and transactions with our management and other related parties is hereby incorporated by reference to such information appearing under the captions "Certain Transactions" and "Compensation Committee Interlocks and Insider Participation" in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2002.

#### *Item 14. Controls and Procedures*

Our chief executive officer and chief financial officer have concluded that our disclosure controls and procedures (as defined in Securities Exchange Act of 1934 Rules 13a-14(c) and 15d-14(c)) are sufficiently effective to ensure that the information required to be disclosed by us in the reports we file under the Securities Exchange Act of 1934 is gathered, analyzed and disclosed with adequate timeliness, accuracy and completeness, based on an evaluation of such controls and procedures conducted within 90 days prior to the date hereof.

Subsequent to our evaluation, there were no significant changes in internal controls or other factors that could significantly affect internal controls, including any corrective actions with regard to significant deficiencies and material weaknesses.

## PART IV

### Item 15. *Exhibits, Financial Statement Schedules and Reports on Form 8-K*

(a) Documents filed as a part of this report:

#### 1. Consolidated Financial Statements

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Report of Independent Auditors .....	F-1
Report of Independent Public Accountants .....	F-2
Consolidated Balance Sheets .....	F-3
Consolidated Statements of Operations .....	F-4
Consolidated Statements of Stockholders' Equity (Deficit) .....	F-5
Consolidated Statements of Cash Flows .....	F-6
Notes to Consolidated Financial Statements .....	F-7

All other financial statement schedules are omitted because they are not applicable or not required, or because the required information is included in the financial statements or notes thereto.

#### 2. Exhibits

<u>Exhibit No.</u>	<u>Description</u>
3.1 —	Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
3.2 —	Restated Bylaws (filed as Exhibit 3.2 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.1 —	Employment Agreement with Arthur T. Sands, M.D., Ph.D. (filed as Exhibit 10.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.2 —	Employment Agreement with James R. Piggott, Ph.D. (filed as Exhibit 10.2 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.3 —	Employment Agreement with Jeffrey L. Wade, J.D. (filed as Exhibit 10.3 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.4 —	Employment Agreement with Brian P. Zambrowicz, Ph.D. (filed as Exhibit 10.4 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.5 —	Employment Agreement with Julia P. Gregory (filed as Exhibit 10.5 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.6 —	Employment Agreement with Randall B. Riggs (filed as Exhibit 10.6 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.7 —	Employment Agreement with Alan Main, Ph.D. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2001 and incorporated by reference herein).

<u>Exhibit No.</u>	<u>Description</u>
10.8	— Employment Agreement with David Boulton (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2001 and incorporated by reference herein).
10.9	— Form of Indemnification Agreement with Officers and Directors (filed as Exhibit 10.7 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.10	— 2000 Equity Incentive Plan (filed as Exhibit 10.8 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.11	— 2000 Non-Employee Directors' Stock Option Plan (filed as Exhibit 10.9 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
10.12	— Coelacanth Corporation 1999 Stock Option Plan (filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 (Registration No. 333-66380) and incorporated by reference herein).
†10.13	— LexVision Database and Collaboration Agreement, dated September 26, 2000, with Bristol-Myers Squibb Company (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated September 26, 2000 and incorporated by reference herein).
†10.14	— LexVision Database and Collaboration Agreement, dated June 27, 2001, with Incyte Genomics, Inc. (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2001 and incorporated by reference herein).
†10.15	— Therapeutic Protein Alliance Agreement, dated June 27, 2001, with Incyte Genomics, Inc. (filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2001 and incorporated by reference herein).
*†10.16	— Collaboration and License Agreement, dated December 17, 2002, with Genentech, Inc.
10.17	— Synthetic Lease Financing Facility with First Security Bank, National Association, the Lenders and Holders named therein, and Bank of America, N.A. (filed as Exhibit 10.12 to the Company's Annual Report on Form 10-K for the year ended December 31, 2000 and incorporated by reference herein).
10.18	— Lease Agreement, dated October 21, 1998, between Coelacanth Chemical Corporation and ARE-279 Princeton Road, LLC. (filed as Exhibit 10.18 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein).
10.19	— Lease Agreement, dated May 23, 2002, between Lexicon Pharmaceuticals (New Jersey), Inc. and Townsend Property Trust Limited Partnership (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2002 and incorporated by reference herein).
21.1	— Subsidiaries (filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein).
*23.1	— Consent of Ernst & Young LLP
*23.2	— Information regarding consent of Arthur Andersen LLP
*24.1	— Power of Attorney (contained in signature page)

Exhibit No.

Description

- |       |   |  |
|-------|---|--|
| 99.1  | — | Letter to the Securities and Exchange Commission regarding Audit Assurances (filed as Exhibit 99.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2001 and incorporated by reference herein). |
| *99.2 | — | Certification of CEO and CFO Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002   |

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\* Filed herewith.

† Confidential treatment has been requested for a portion of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

(b) Reports on Form 8-K:

None.

## Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

### Lexicon Genetics Incorporated

Date: March 17, 2003

By: /s/ ARTHUR T. SANDS  
 Arthur T. Sands, M.D., Ph.D.  
*President and Chief Executive Officer*

Date: March 17, 2003

By: /s/ JULIA P. GREGORY  
 Julia P. Gregory  
*Executive Vice President and  
 Chief Financial Officer*

## Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Julia P. Gregory and Jeffrey L. Wade, or either of them, each with the power of substitution, his or her attorney-in-fact, to sign any amendments to this Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, here ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ ARTHUR T. SANDS</u> Arthur T. Sands, M.D., Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	March 17, 2003
<u>/s/ JULIA P. GREGORY</u> Julia P. Gregory	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2003
<u>/s/ C. THOMAS CASKEY</u> C. Thomas Caskey, M.D.	Chairman of the Board of Directors	March 17, 2003
<u>/s/ SAM L. BARKER</u> Sam L. Barker, Ph.D.	Director	March 17, 2003
<u>/s/ PATRICIA M. CLOHERTY</u> Patricia M. Cloherty	Director	March 17, 2003
<u>/s/ ROBERT J. LEFKOWITZ</u> Robert J. Lefkowitz, M.D.	Director	March 17, 2003
<u>/s/ WILLIAM A. MCMINN</u> William A. McMinn	Director	March 17, 2003

## Certifications

I, Arthur T. Sands, certify that:

1. I have reviewed this annual report on Form 10-K of Lexicon Genetics Incorporated;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Securities Exchange Act of 1934 Rules 13a-14 and 15d-14) for the registrant and have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date.
5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls.
6. The registrant's other certifying officers and I have indicated in this annual report whether there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 17, 2003

/s/ ARTHUR T. SANDS

Arthur T. Sands, M.D., Ph.D.

President and Chief Executive Officer

I, Julia P. Gregory, certify that:

1. I have reviewed this annual report on Form 10-K of Lexicon Genetics Incorporated;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in the Securities Exchange Act of 1934 Rules 13a-14 and 15d-14) for the registrant and have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date.
5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls.
6. The registrant's other certifying officers and I have indicated in this annual report whether there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 17, 2003

/s/ JULIA P. GREGORY

Julia P. Gregory

Executive Vice President and Chief Financial Officer



## Report of Independent Auditors

To the Board of Directors and Stockholders  
of Lexicon Genetics Incorporated:

We have audited the accompanying consolidated balance sheet of Lexicon Genetics Incorporated and subsidiary (the Company) as of December 31, 2002, and the related consolidated statement of operations, stockholders' equity (deficit) and cash flow for the year then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit. The financial statements of the Company as of December 31, 2001 and 2000, and for the years then ended were audited by other auditors who have ceased operations and whose report dated February 22, 2002 expressed an unqualified opinion on those statements before the reclassification adjustments and conforming disclosures described in Note 4.

We conducted our audit in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Lexicon Genetics Incorporated as of December 31, 2002, and the consolidated results of its operations and its cash flows for the year then ended, in conformity with accounting principles generally accepted in the United States.

As discussed above, the financial statements of the Company as of December 31, 2001 and 2000, and for the years then ended were audited by other auditors who have ceased operations. As described in Note 4, these financial statements have been revised. We audited the reclassification adjustments and conforming disclosures described in Note 4 that were applied to revise the 2001 and 2000 financial statements. In our opinion, such reclassification adjustments and conforming disclosures are appropriate and have been properly applied. However, we were not engaged to audit, review or apply any procedures to the 2001 and 2000 financial statements of the Company other than with respect to such reclassification adjustments and conforming disclosures and, accordingly, we do not express an opinion or any other form of assurance on the 2001 and 2000 financial statements taken as a whole.

/s/ ERNST & YOUNG LLP

Houston, Texas  
February 13, 2003

## Report of Independent Public Accountants

To the Board of Directors and Stockholders  
of Lexicon Genetics Incorporated:

We have audited the accompanying consolidated balance sheets of Lexicon Genetics Incorporated (a Delaware corporation) and subsidiary as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2001. These financial statements are the responsibility of Lexicon Genetics Incorporated's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Lexicon Genetics Incorporated and subsidiary as of December 31, 2001 and 2000, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

ARTHUR ANDERSEN LLP

Houston, Texas  
February 22, 2002

This is a copy of the report issued by Arthur Andersen LLP, Lexicon's former independent public accountants, in connection with the Company's annual report on Form 10-K for the year ended December 31, 2001. This report has not been reissued by Arthur Andersen LLP in connection with Lexicon's annual report on Form 10-K for the year ended December 31, 2002. See Exhibit 23.2 for further information.

Lexicon Genetics Incorporated

Consolidated Balance Sheets  
(In thousands, except par value)

	As of December 31,	
	2002	2001
<u>Assets</u>		
Current assets:		
Cash and cash equivalents .....	\$ 39,362	\$ 16,355
Restricted cash .....	29,487	6,693
Short-term investments, including restricted investments of \$28,223 and \$36,645, respectively .....	54,247	133,394
Accounts receivable, net of allowance for doubtful accounts of \$109 and \$211, respectively .....	5,143	4,544
Prepaid expenses and other current assets .....	4,893	5,456
Total current assets .....	133,132	166,442
Property and equipment, net of accumulated depreciation of \$19,768 and \$10,747, respectively .....	37,362	26,707
Long-term investments .....	—	10,398
Goodwill .....	25,798	25,798
Intangible assets, net of amortization of \$1,760 and \$560, respectively .....	4,240	5,440
Other assets .....	1,240	5,205
Total assets .....	<u>\$ 201,772</u>	<u>\$ 239,990</u>
<u>Liabilities and Stockholders' Equity</u>		
Current liabilities:		
Accounts payable .....	\$ 4,378	\$ 3,168
Accrued liabilities .....	4,161	5,016
Current portion of deferred revenue .....	12,760	10,595
Total current liabilities .....	21,299	18,779
Deferred revenue, net of current portion .....	5,887	2,500
Long-term debt .....	4,000	—
Other long-term liabilities .....	684	339
Total liabilities .....	31,870	21,618
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$.01 par value; 5,000 shares authorized; no shares issued and outstanding .....	—	—
Common stock, \$.001 par value; 120,000 shares authorized; 52,367 and 52,022 shares issued and outstanding, respectively .....	52	52
Additional paid-in capital .....	330,701	331,092
Deferred stock compensation .....	(11,106)	(22,260)
Accumulated deficit .....	(149,745)	(90,075)
Accumulated other comprehensive loss .....	—	(437)
Total stockholders' equity .....	169,902	218,372
Total liabilities and stockholders' equity .....	<u>\$ 201,772</u>	<u>\$ 239,990</u>

The accompanying notes are an integral part of these consolidated financial statements.

Lexicon Genetics Incorporated

Consolidated Statements of Operations  
(In thousands, except per share amounts)

	Year Ended December 31,		
	2002	2001	2000
Revenues:			
Subscription and license fees.....	\$ 17,871	\$ 14,744	\$ 4,579
Collaborative research .....	17,088	11,220	9,505
Compound libraries and other .....	<u>241</u>	<u>4,613</u>	<u>375</u>
Total revenues.....	35,200	30,577	14,459
Operating expenses:			
Research and development, including stock-based compensation of \$5,155, \$5,539 and \$10,883, respectively.....	74,859	53,355	31,647
General and administrative, including stock-based compensation of \$5,113, \$5,231 and \$9,958, respectively.....	<u>23,234</u>	<u>20,861</u>	<u>18,289</u>
Total operating expenses.....	<u>98,093</u>	<u>74,216</u>	<u>49,936</u>
Loss from operations .....	(62,893)	(43,639)	(35,477)
Interest and other income.....	3,230	8,781	9,905
Interest expense .....	<u>(7)</u>	<u>(314)</u>	<u>(422)</u>
Net loss .....	(59,670)	(35,172)	(25,994)
Accretion on redeemable convertible preferred stock .....	<u>—</u>	<u>—</u>	<u>(134)</u>
Net loss attributable to common stockholders .....	<u>\$ (59,670)</u>	<u>\$ (35,172)</u>	<u>\$ (26,128)</u>
Net loss per common share, basic and diluted .....	<u>\$ (1.14)</u>	<u>\$ (0.70)</u>	<u>\$ (0.63)</u>
Shares used in computing net loss per common share, basic and diluted .....	52,263	50,213	41,618

*The accompanying notes are an integral part of these consolidated financial statements.*

**Lexicon Genetics Incorporated**  
**Consolidated Statements of Stockholders' Equity (Deficit)**  
(In thousands)

	<u>Common Stock</u>		<u>Additional</u>	<u>Deferred</u>	<u>Accumulated</u>	<u>Accumulated</u>	<u>Total</u>
	<u>Shares</u>	<u>Par Value</u>	<u>Paid-In</u>	<u>Stock</u>	<u>Deficit</u>	<u>Other</u>	<u>Stockholders'</u>
			<u>Capital</u>	<u>Compensation</u>		<u>Comprehensive</u>	<u>Equity (Deficit)</u>
						<u>Loss</u>	
Balance at December 31, 1999.....	24,540	\$ 24	\$ 7,863	\$ (915)	\$ (28,909)	\$ —	\$ (21,937)
Initial public offering of common stock ..	10,000	10	203,175	—	—	—	203,185
Accretion on redeemable convertible preferred stock to redemption value ....	—	—	(134)	—	—	—	(134)
Conversion of redeemable convertible preferred stock to common stock .....	12,734	13	30,171	—	—	—	30,184
Deferred stock compensation, net of reversals .....	—	—	53,563	(53,563)	—	—	—
Amortization of deferred stock compensation .....	—	—	—	20,841	—	—	20,841
Exercise of common stock options .....	849	1	1,111	—	—	—	1,112
Exercise of common stock warrants .....	149	—	371	—	—	—	371
Net loss .....	—	—	—	—	(25,994)	—	(25,994)
Balance at December 31, 2000.....	48,272	48	296,120	(33,637)	(54,903)	—	207,628
Deferred stock compensation, net of reversals .....	—	—	(958)	958	—	—	—
Deferred stock compensation of options assumed in acquisition .....	—	—	—	(351)	—	—	(351)
Amortization of deferred stock compensation .....	—	—	—	10,770	—	—	10,770
Common stock issued in connection with acquisition .....	2,919	3	35,213	—	—	—	35,216
Exercise of common stock options .....	419	1	717	—	—	—	718
Exercise of common stock warrants .....	412	—	—	—	—	—	—
Net loss .....	—	—	—	—	(35,172)	—	(35,172)
Unrealized loss on long-term investments .....	—	—	—	—	—	(437)	(437)
Comprehensive loss .....	—	—	—	—	—	—	(35,609)
Balance at December 31, 2001 .....	52,022	52	331,092	(22,260)	(90,075)	(437)	218,372
Deferred stock compensation, net of reversals .....	—	—	(985)	985	—	—	—
Issuance of restricted stock .....	18	—	99	(99)	—	—	—
Amortization of deferred stock compensation .....	—	—	—	10,268	—	—	10,268
Cancellation of equity securities in connection with acquisition .....	(7)	—	(79)	—	—	—	(79)
Exercise of common stock options .....	330	—	574	—	—	—	574
Exercise of common stock warrants .....	4	—	—	—	—	—	—
Net loss .....	—	—	—	—	(59,670)	—	(59,670)
Reversal of unrealized loss on sale of long-term investments .....	—	—	—	—	—	437	437
Comprehensive loss .....	—	—	—	—	—	—	(59,233)
Balance at December 31, 2002.....	<u>52,367</u>	<u>\$ 52</u>	<u>\$ 330,701</u>	<u>\$ (11,106)</u>	<u>\$ (149,745)</u>	<u>\$ —</u>	<u>\$ 169,902</u>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Lexicon Genetics Incorporated**  
**Consolidated Statements of Cash Flows**  
(In thousands)

	Year Ended December 31,		
	2002	2001	2000
<b>Cash flows from operating activities</b>			
Net loss .....	\$ (59,670)	\$ (35,172)	\$ (25,994)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation .....	9,111	5,220	2,621
Amortization of intangible assets, other than goodwill .....	1,200	560	—
Amortization of deferred stock compensation .....	10,268	10,770	20,841
Loss on sale of long-term investments .....	197	—	—
Changes in operating assets and liabilities:			
(Increase) decrease in accounts receivable .....	(599)	(1,409)	577
(Increase) decrease in prepaid expenses and other current assets .....	484	(2,531)	(460)
(Increase) decrease in other assets .....	3,965	(4,919)	97
Increase in accounts payable and other liabilities .....	700	1,089	4,354
Increase (decrease) in deferred revenue .....	<u>5,552</u>	<u>8,402</u>	<u>(3,538)</u>
Net cash used in operating activities .....	(28,792)	(17,990)	(1,502)
<b>Cash flows from investing activities</b>			
Purchases of property and equipment .....	(19,766)	(13,471)	(7,709)
(Increase) decrease in restricted cash .....	(22,794)	7,186	(13,879)
Purchase of short-term investments .....	(91,962)	(355,869)	(269,847)
Maturities of short-term investments .....	171,109	387,345	112,108
Purchase of long-term investments .....	—	(10,835)	—
Sale of long-term investments .....	10,638	—	—
Payment of transaction costs, net of cash acquired .....	<u>—</u>	<u>(752)</u>	<u>—</u>
Net cash provided by (used in) investing activities .....	47,225	13,604	(179,327)
<b>Cash flows from financing activities</b>			
Principal payments on capital lease obligations .....	—	—	(133)
Proceeds from debt borrowings .....	4,000	—	—
Repayment of debt borrowings .....	—	(3,909)	(1,462)
Proceeds from issuance of common stock .....	<u>574</u>	<u>718</u>	<u>204,330</u>
Net cash provided by (used in) financing activities .....	<u>4,574</u>	<u>(3,191)</u>	<u>202,735</u>
Net increase (decrease) in cash and cash equivalents .....	23,007	(7,577)	21,906
Cash and cash equivalents at beginning of year .....	<u>16,355</u>	<u>23,932</u>	<u>2,026</u>
Cash and cash equivalents at end of year .....	<u>\$ 39,362</u>	<u>\$ 16,355</u>	<u>\$ 23,932</u>
<b>Supplemental disclosure of cash flow information</b>			
Cash paid for interest .....	\$ 7	\$ 330	\$ 422
<b>Supplemental disclosure of noncash investing and financing activities</b>			
Unrealized loss on long-term investments .....	\$ —	\$ (437)	\$ —
Reversal of unrealized loss on sale of long-term investments .....	\$ 437	\$ —	\$ —
Conversion of redeemable convertible preferred stock into common stock .....	\$ —	\$ —	\$ 30,184
Conversion of related party note payable into common stock .....	\$ —	\$ —	\$ 338
Issuance of equity securities in connection with acquisition .....	\$ —	\$ 35,216	\$ —
Cancellation of equity securities in connection with acquisition .....	\$ (79)	\$ —	\$ —
Deferred stock compensation, net of reversals .....	\$ 985	\$ 958	\$ (53,563)
Deferred stock compensation in connection with issuance of restricted stock .....	\$ (99)	\$ —	\$ —
Retirement of property and equipment .....	\$ 90	\$ 181	\$ —

*The accompanying notes are an integral part of these consolidated financial statements.*

Lexicon Genetics Incorporated  
Notes to Consolidated Financial Statements

December 31, 2002

1. Organization and Operations

Lexicon Genetics Incorporated (Lexicon or the Company) is a Delaware corporation incorporated on July 7, 1995. Lexicon was organized to discover the functions and pharmaceutical utility of genes and use those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease.

Lexicon has financed its operations from inception primarily through sales of common and preferred stock, contract and milestone payments received under subscription and collaboration agreements, equipment financing arrangements and leasing arrangements. The Company's future success is dependent upon many factors, including, but not limited to, its ability to discover promising candidates for drug target or therapeutic protein development using its gene knockout technology, establish additional research contracts and agreements for access to its technology, achieve milestones under such contracts and agreements, obtain and enforce patents and other proprietary rights in its discoveries, comply with federal and state regulations, and maintain sufficient capital to fund its activities. As a result of the aforementioned factors and the related uncertainties, there can be no assurance of the Company's future success.

2. Summary of Significant Accounting Policies

*Basis of Presentation:* The accompanying consolidated financial statements include the accounts of Lexicon and its subsidiary. Intercompany transactions and balances are eliminated in consolidation.

*Use of Estimates:* The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the period. Actual results could differ from those estimates.

*Cash, Cash Equivalents, Short-term Investments and Long-term Investments:* Lexicon considers all highly-liquid investments with original maturities or auction-based interest rate reset dates of three months or less to be cash equivalents. Management determines the appropriate classification of its cash equivalents, short-term investments and long-term investments at the time of purchase. Short-term investments consist of U.S. government agency debt obligations, investment grade commercial paper, corporate debt securities and certificates of deposit that have maturities of three to twelve months from the date of purchase. Short-term investments are classified as held-to-maturity securities in the accompanying financial statements. Held-to-maturity securities are carried at amortized cost. Long-term investments at December 31, 2001 consist of a U.S. government agency debt obligation with a maturity greater than twelve months from the time of purchase. Long-term investments are classified as available-for-sale securities and, accordingly, are stated at fair value based upon quoted market prices of the securities. Unrealized gains and losses on such securities are reported as other comprehensive income (loss), which is a separate component of stockholders' equity. In 2002, the Company sold its available-for-sale securities. As a result, there is no unrealized gain (loss) as of December 31, 2002.

*Restricted Cash and Investments:* Lexicon is required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement under which it leases its office and laboratory facilities in The Woodlands, Texas as well as to collateralize standby letters of credit for the leases on its office and laboratory facilities in East Windsor and Hopewell, New Jersey (see Note 10). As of December 31, 2002 and 2001, the Company maintained restricted cash and investments of \$57.7 million and \$43.3 million, respectively, under these agreements.

*Concentration of Credit Risk:* Lexicon's cash equivalents, short-term investments and trade receivables represent potential concentrations of credit risk. The Company minimizes potential concentrations of risk in cash equivalents and short-term investments by placing investments in high-quality financial instruments. The Company's customers are primarily pharmaceutical and biotechnology companies located in the United States and Europe. The Company has not experienced any significant credit losses to date and, at December 31, 2002, management believes that the Company has no significant concentrations of credit risk.

*Segment Information and Significant Customers:* Lexicon operates in one business segment, which primarily focuses on the discovery of the functions and pharmaceutical utility of genes and the use of those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease. Substantially all of the Company's revenues have been derived from subscriptions to its databases, drug discovery alliances, functional genomics collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales. In 2002, Incyte Genomics, Inc., Bristol-Myers Squibb Company and Millennium Pharmaceuticals, Inc. represented 28%, 14% and 11% of revenues, respectively. In 2001, Incyte, Bristol-Myers Squibb and Merck & Co., Inc. represented 16%, 13% and 12% of revenues, respectively. In 2000, the Merck Genome Research Institute and Millennium represented 35% and 14% of revenues, respectively.

*Property and Equipment:* Property and equipment are carried at cost and depreciated using the straight-line method over the estimated useful life of the assets which ranges from three to ten years. Maintenance, repairs and minor replacements are charged to expense as incurred. Significant renewals and betterments are capitalized.

*Impairment of Long-Lived Assets:* Long-lived assets and certain identifiable intangible assets to be held and used are reviewed for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values.

*Goodwill Impairment:* Under Statement of Financial Accounting Standards (SFAS) No. 142, "Goodwill and Other Intangible Assets," goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if the Company encounters events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2002.

*Revenue Recognition:* Revenues are recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned. Revenues are earned from database subscriptions, drug discovery alliances, functional genomics collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales.

Fees for access to databases and other functional genomics resources are recognized ratably over the subscription or access period. Collaborative research payments are recognized as revenue as Lexicon performs its obligations related to such research to the extent such fees are non-refundable. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Non-refundable technology license fees are recognized as revenue upon the grant of the license when performance is complete and there is no continuing involvement. Compound library sales are recognized as revenue upon shipment.

Revenues recognized from multiple element contracts are allocated to each element of the arrangement based on the relative fair values of the elements. The determination of fair value of each element is based on objective evidence. In accordance with Staff Accounting Bulletin No. 101 "Revenue Recognition in Financial Statements," when revenues for an element are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligation associated with the element is completed. When revenues for an element are not specifically tied to a separate earnings process, they are recognized ratably over the term of the agreement.

*Research and Development Expenses:* Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Patent costs and technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.



*Stock-based Compensation:* As further discussed in Note 12, Lexicon has three stock-based compensation plans, which are accounted for under the recognition and measurement provisions of Accounting Principles Board (APB) Opinion No. 25, "Accounting for Stock Issued to Employees, and Related Interpretations." Under the intrinsic value method described in APB Opinion No. 25, no compensation expense is recognized if the exercise price of the employee stock option equals the market price of the underlying stock on the date of grant. Lexicon recognized \$10.3 million, \$10.8 million and \$20.8 million of stock-based compensation during 2002, 2001 and 2000, respectively, which was primarily related to option grants made prior to Lexicon's April 2000 initial public offering. The following table illustrates the effect on net loss and net loss per share if the fair value recognition provisions of Financial Accounting Standards Board (FASB) No. 123 "Accounting for Stock Based Compensation," had been applied to all outstanding and unvested awards in each period:

	Year Ended December 31,		
	2002	2001 (in thousands)	2000
Net loss, as reported.....	\$ (59,670)	\$ (35,172)	\$ (25,994)
Add: Stock-based employee compensation expense included in reported net loss .....	10,268	10,770	20,841
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards .....	(25,913)	(20,616)	(27,346)
Pro forma net loss .....	<u>\$ (75,315)</u>	<u>\$ (45,018)</u>	<u>\$ (32,499)</u>
Net loss per common share, basic and diluted			
As reported .....	<u>\$ (1.14)</u>	<u>\$ (0.70)</u>	<u>\$ (0.63)</u>
Pro forma .....	<u>\$ (1.44)</u>	<u>\$ (0.90)</u>	<u>\$ (0.78)</u>

*Net Loss Per Common Share:* Net loss per common share is computed using the weighted average number of shares of common stock outstanding. Shares associated with stock options, warrants and convertible preferred stock are not included because they are antidilutive.

*Comprehensive Loss:* Comprehensive loss is comprised of net loss and unrealized gains and losses on long-term investments, which are considered available-for-sale securities. Comprehensive loss is reflected in the consolidated statements of stockholders' equity. During 2002, Lexicon sold its available-for-sale securities for \$10.6 million, resulting in a realized loss of \$197,000 reflected in its net loss for the year. As a result, there is no accumulated other comprehensive loss as of December 31, 2002.

### 3. Recent Accounting Pronouncements

In November 2002, the Financial Accounting Standards Board (FASB) issued Interpretation (FIN) No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others." FIN 45 elaborates on the existing disclosure requirements for most guarantees, including residual value guarantees issued in conjunction with operating lease agreements. It also clarifies that at the time a company issues a guarantee, the company must recognize an initial liability for the fair value of the obligation it assumes under that guarantee and must disclose that information in its interim and annual financial statements. The initial recognition and measurement provisions apply on a prospective basis to guarantees issued or modified after December 31, 2002. The disclosure requirements are effective for financial statements of interim or annual periods ending after December 15, 2002. The adoption of FIN 45 will not have a material impact on Lexicon's results of operations and financial position. See Note 10 regarding disclosures on residual value guarantees and Lexicon's exposure related to its synthetic lease and standby letters of credit related to other operating leases.

In November 2002, the Emerging Issues Task Force (EITF) reached a consensus on EITF Issue No. 00-21 "Accounting for Revenue Arrangements with Multiple Deliverables." This issue requires that revenue arrangements with multiple deliverables be divided into separate units of accounting if the deliverables meet the following criteria: the delivered items have value to the customer on a standalone basis; there is objective and reliable evidence of fair value of the undelivered items; and, if the arrangement includes a general right of return, performance of the undelivered item is considered probable and substantially in control of Lexicon. The final consensus will be applicable to agreements entered into in fiscal periods beginning after June 15, 2003 with early adoption permitted.

In December 2002, the FASB issued SFAS 148, "Accounting for Stock-Based Compensation – Transition and Disclosure." This statement amends SFAS 123, "Accounting for Stock-Based Compensation," to provide

alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, this statement amends the disclosure requirements of SFAS 123 to require prominent disclosures in both annual and interim financial statements about the method of accounting for stock-based employee compensation and the effect of the method used on reported results. The Company is currently evaluating whether to adopt the fair value based method. The additional disclosures required under SFAS 148 are effective for fiscal years ending after December 15, 2002, and have been provided in Note 2.

In January 2003, the FASB issued FIN 46, "Consolidation of Variable Interest Entities." FIN 46 requires that unconsolidated variable interest entities be consolidated by their primary beneficiaries. A primary beneficiary is the party that absorbs a majority of the entity's expected losses or residual benefits. FIN 46 applies immediately to variable interest entities created after January 31, 2003 and to existing variable interest entities in the periods beginning after June 15, 2003. The Company is evaluating whether the adoption of FIN 46 will require the consolidation of the lessor under its synthetic lease, discussed in Note 10. If such consolidation is required, the Company's balance sheet will reflect as assets additional property and equipment approximating the \$55.0 million funded under the synthetic lease for property and improvements, less accumulated depreciation, and a similar amount as a liability. In addition, the Company will be required to depreciate such improvements over their useful lives. The Company may, however, elect to restructure or replace the synthetic lease prior to the adoption of FIN 46, whether or not such consolidation would be required.

#### 4. Reclassifications and Conforming Disclosures

In the accompanying balance sheet as of December 31, 2001, Lexicon has reclassified the amount of restricted cash from cash and cash equivalents into a separate line item. The accompanying statements of cash flows for the years ended December 31, 2001 and 2000 have also been revised to reflect this reclassification. Additionally, Lexicon included disclosures at December 31, 2001 in a table in Note 5 to conform the prior year information to the current year presentation.

#### 5. Investments

Investments at December 31, 2002 and 2001 were as follows:

	As of December 31, 2002			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Held-to-maturity:				
Certificates of deposit.....	\$ 6,091	\$ —	\$ —	\$ 6,091
U.S. government agencies .....	7,036	5	—	7,041
Corporate debt securities .....	13,719	8	(3)	13,724
Commercial paper .....	26,127	—	—	26,127
Other debt securities .....	1,274	7	—	1,281
Total held-to-maturity investments.....	<u>\$ 54,247</u>	<u>\$ 20</u>	<u>\$ (3)</u>	<u>\$ 54,264</u>
	As of December 31, 2001			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Held-to-maturity:				
Certificates of deposit.....	\$ 11,221	\$ —	\$ —	\$ 11,221
U.S. government agencies .....	24,125	23	(16)	24,132
Corporate debt securities .....	33,568	107	(26)	33,649
Commercial paper .....	64,480	6	—	64,486
Total held-to-maturity investments.....	<u>\$ 133,394</u>	<u>\$ 136</u>	<u>\$ (42)</u>	<u>\$ 133,488</u>
Available-for-sale:				
U.S. government agencies .....	<u>\$ 10,835</u>	<u>\$ —</u>	<u>\$ (437)</u>	<u>\$ 10,398</u>
Total available-for-sale investments.....	<u>\$ 10,835</u>	<u>\$ —</u>	<u>\$ (437)</u>	<u>\$ 10,398</u>

## 6. Property and Equipment

Property and equipment at December 31, 2002 and 2001 are as follows:

	Estimated Useful Lives In Years	As of December 31,	
		2002	2001
		(In thousands)	
Computers and software .....	3-5	\$ 10,996	\$ 8,659
Furniture and fixtures.....	5-7	8,595	5,044
Laboratory equipment.....	3-7	27,282	17,000
Leasehold improvements .....	3-10	10,257	6,751
Total property and equipment.....		57,130	37,454
Less: Accumulated depreciation .....		(19,768)	(10,747)
Net property and equipment .....		\$ 37,362	\$ 26,707

## 7. Income Taxes

Lexicon recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently in the financial statements and tax returns. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax bases of liabilities and assets using enacted tax rates and laws in effect in the years in which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on a more-likely-than-not criteria in determining if a valuation should be provided.

The components of Lexicon's deferred tax assets (liabilities) at December 31, 2002 and 2001 are as follows:

	As of December 31,	
	2002	2001
(In thousands)		
Deferred tax assets:		
Net operating loss carryforwards .....	\$ 39,887	\$ 14,535
Research and development tax credits .....	7,113	4,607
Stock-based compensation .....	5,828	4,307
Accrued expenses and other .....	5,916	5,550
Total deferred tax assets .....	58,744	28,999
Deferred tax liabilities:		
Property and equipment .....	(990)	(341)
Other .....	(138)	(18)
Total deferred tax liabilities .....	(1,128)	(359)
Less: Valuation allowance .....	(57,616)	(28,640)
Net deferred tax assets .....	<u>\$ —</u>	<u>\$ —</u>

At December 31, 2002, Lexicon had net operating loss carryforwards of approximately \$114.0 million and research and development tax credit carryforwards of approximately \$7.1 million available to reduce future income taxes. These carryforwards will begin to expire in 2011. A change in ownership, as defined by federal income tax regulations, could significantly limit the Company's ability to utilize its carryforwards. Based on the federal tax law limits and the Company's cumulative loss position, Lexicon concluded it was appropriate to establish a full valuation allowance for its net deferred tax assets until an appropriate level of profitability is sustained. During 2002, the valuation allowance increased \$29.0 million primarily due to the Company's current year net loss, the acquired net operating loss carryforwards from the purchase of Coelacanth Corporation, and the current year research tax credits.

## 8. Goodwill and Other Intangible Assets

On July 12, 2001, Lexicon completed the acquisition of Coelacanth Corporation in a merger. Coelacanth, now Lexicon Pharmaceuticals (New Jersey), Inc., forms the core of Lexicon Pharmaceuticals, the division of the

Company responsible for small molecule compound discovery. The results of Lexicon Pharmaceuticals (New Jersey), Inc. are included in the Company's results of operations for the period subsequent to the acquisition.

Goodwill, associated with the acquisition, of \$25.8 million, which represents the excess of the \$36.0 million purchase price over the fair value of the underlying net identifiable assets, was assigned to the consolidated entity, Lexicon. There were no changes in the carrying amount of goodwill for the year ended December 31, 2002. In accordance with SFAS 142, the goodwill balance is not subject to amortization, but is tested at least annually for impairment. The Company performed an impairment test of goodwill upon adoption of SFAS 142 and on its annual impairment assessment date. This comparison did not result in an impairment of goodwill at either assessment date.

Other intangible assets represent Coelacanth's technology platform, which consists of its proprietary ClickChem<sup>™</sup> reactions, novel building blocks and compound sets, automated production systems, high throughput ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) capabilities and its know-how and trade secrets. The Company expects to amortize the value assigned to other intangible assets on a straight-line basis over an estimated life of five years.

The amortization expense for the year ended December 31, 2002 was \$1.2 million. The estimated amortization expense for the next five years is as follows:

	For the Year Ending December 31	
	(In thousands)	
2003 .....	\$	1,200
2004 .....		1,200
2005 .....		1,200
2006 .....		640
2007 .....	\$	—

## 9. Debt Obligations

On December 31, 2002, Lexicon borrowed \$4.0 million under a note agreement with Genentech, Inc. The proceeds of the loan are to be used to fund research efforts under the alliance agreement with Genentech discussed in Note 14. The note matures on or before December 31, 2005, but the Company may prepay it at any time. The Company may repay the note, at its option, in cash, in shares of common stock valued at the then-current market price, or in a combination of cash and shares, subject to certain limitations. The note accrues interest at an annual rate of 8%, compounded quarterly. The note is subordinated in right of payment to borrowings made under Lexicon's synthetic lease, which is discussed in Note 10.

## 10. Commitments and Contingencies

**Lease Obligations:** In October 2000, Lexicon entered into a synthetic lease agreement under which the lessor purchased the Company's existing laboratory and office buildings and animal facility in The Woodlands, Texas and agreed to fund the construction of an additional laboratory and office building and a second animal facility. The synthetic lease agreement was subsequently expanded to include funding for the construction of a central plant facility. Including the purchase price for the Company's existing facilities, the synthetic lease, as amended, provides for funding of up to \$55.0 million in property and improvements. The term of the agreement is six years, which includes the construction period and a lease period. Lease payments for the new facilities began upon completion of construction, which occurred at the end of the first quarter of 2002. Lease payments are subject to fluctuation based on LIBOR rates. Based on a year-end LIBOR rate of 1.4% the Company's total lease payments would be approximately \$0.9 million per year. At the end of the lease term, the lease may be extended for one-year terms, up to seven additional terms, or the Company may purchase the properties for a price equal to the \$55.0 million funded under the synthetic lease for property and improvements plus the amount of any accrued but unpaid lease payments. If the Company elects not to renew the lease or purchase the properties, it may arrange for the sale of the properties to a third party or surrender the properties to the lessor. If the Company elects to arrange for the sale of the properties or surrender the properties to the lessor, it has guaranteed approximately 86% of the total original cost as the residual fair value of the properties. The Company is required to maintain restricted cash or investments to collateralize borrowings made under the synthetic lease agreement. In addition, Lexicon has agreed to maintain cash and investments of at least \$12.0 million in excess of the Company's restricted cash and investments. If the Company's cash and investments fall below that level, the Company may be required to seek a waiver of that agreement or to purchase the properties or arrange for their sale to a third party. Because the Company's cost to

purchase the properties would not materially exceed the \$55.0 million funded under the synthetic lease for property and improvements and would likely be less than the amount of restricted cash and investments it is required to maintain under the synthetic lease, the Company believes that any requirement that it do so would not have a material adverse effect on its financial condition. As of December 31, 2002 and 2001, the Company maintained restricted cash and investments of \$57.2 million and \$43.3 million, respectively, to collateralize funding for property and improvements under the synthetic lease of \$55.0 million and \$41.7 million.

Lexicon's subsidiary leases laboratory and office space in East Windsor, New Brunswick and Hopewell, New Jersey under agreements which expire in January 2004, January 2003 and May 2012, respectively. The Hopewell lease is a ten-year lease for a 76,000 square-foot facility in New Jersey. The lease provides for an escalating yearly rent payment of \$1.3 million in the first year, \$1.7 million in years two and three, \$1.8 million in years four to six, \$2.0 million in years seven to nine and \$2.1 million in year ten. The lease also provides an option in the second year of the lease to borrow \$2.0 million in tenant improvement funds from the landlord, at which time rental payments due under the lease will increase as the tenant improvement allowance is amortized over a ten-year period. Lexicon is the guarantor of the obligations of its subsidiary under the lease. The Company is required to maintain restricted investments to collateralize the East Windsor and Hopewell leases. As of December 31, 2002, the Company had \$0.5 million in restricted investments to collateralize standby letters of credit for these leases. Additionally, Lexicon leases certain equipment under operating leases.

Rent expense for all operating leases was approximately \$2.8 million, \$0.9 million, and \$1.5 million for the years ended December 31, 2002, 2001 and 2000, respectively. The table below includes non-cancelable future lease payments for the facilities in The Woodlands, Texas based on a year-end LIBOR rate of 1.4%, as well as future lease payments for the facilities in New Jersey:

	For the Year Ending December 31 (In thousands)
2003 .....	\$ 3,479
2004 .....	2,796
2005 .....	2,805
2006 .....	2,769
2007 .....	1,904
Thereafter .....	8,953
Total .....	<u>\$ 22,706</u>

*Employment Agreements:* Lexicon has entered into employment agreements with certain of its corporate officers. Under the agreements, each officer receives a base salary, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreements are at-will and contain non-competition agreements. The agreements also provide for a termination clause, which requires either a six or 12-month payment based on the officer's salary, in the event of termination or change in corporate control.

## 11. Capital Stock

*Stock Dividend:* Lexicon's Board of Directors declared a stock dividend to effect a stock split of three shares for every one share of common stock then outstanding, effective April 5, 2000. The accompanying financial statements and footnotes give retroactive effect to the stock split for all periods presented.

*Common Stock:* In April 2000, Lexicon completed the initial public offering of 10,000,000 shares of its common stock at an initial public offering price of \$22.00 per share, for net proceeds of \$203.2 million, after deducting underwriting discounts of \$15.4 million and offering expenses of \$1.4 million.

*Redeemable Convertible Series A Preferred Stock:* Lexicon's redeemable convertible Series A preferred stock, originally issued in a private placement in May 1998, was converted according to its terms into 12,733,992 shares of common stock upon the April 2000 closing of the Company's initial public offering of common stock. Prior to the conversion, the Series A preferred stock was being accreted to its May 7, 2003 redemption value of \$31.8 million. The Series A preferred stock was not included as a component of total stockholders' equity (deficit) due to its redemption features.

## 12. Stock Options and Warrants

### *Stock Options*

**2000 Equity Incentive Plan:** In September 1995, Lexicon adopted the 1995 Stock Option Plan, which was subsequently amended and restated in February 2000 as the 2000 Equity Incentive Plan (the "Equity Incentive Plan"). The Equity Incentive Plan will terminate in 2010 unless the Board of Directors terminates it sooner. The Equity Incentive Plan provides that it will be administered by the Board of Directors, or a committee appointed by the Board of Directors, which determines recipients and types of options to be granted, including number of shares under the option and the exercisability of the shares. The Equity Incentive Plan is presently administered by the Compensation Committee of the Board of Directors.

The Equity Incentive Plan provides for the grant of incentive stock options to employees and nonstatutory stock options to employees, directors and consultants of the Company. The plan also permits the grant of stock bonuses and restricted stock purchase awards. Incentive stock options have an exercise price of 100% or more of the fair market value of our common stock on the date of grant. Nonstatutory stock options may have an exercise price as low as 85% of fair market value on the date of grant. The purchase price of other stock awards may not be less than 85% of fair market value. However, the plan administrator may award bonuses in consideration of past services without a purchase payment. Shares may be subject to a repurchase option in the discretion of the plan administrator.

The Board of Directors initially authorized and reserved an aggregate of 11,250,000 shares of common stock for issuance under the Equity Incentive Plan. On January 1 of each year for ten years, beginning in 2001, the number of shares reserved for issuance under the Equity Incentive Plan automatically will be increased by the greater of:

- 5% of Lexicon's outstanding shares on a fully-diluted basis; or
- that number of shares that could be issued under awards granted under the Equity Incentive Plan during the prior 12-month period;

provided that the Board of Directors may provide for a lesser increase in the number of shares reserved under the Equity Incentive Plan for any year. The total number of shares reserved in the aggregate may not exceed 60,000,000 shares over the ten-year period.

As of December 31, 2002, an aggregate of 14,500,000 shares of common stock had been reserved for issuance, options to purchase 11,201,000 shares were outstanding and 1,693,000 shares had been issued upon the exercise of stock options issued under the Equity Incentive Plan.

**2000 Non-Employee Directors' Stock Option Plan:** In February 2000, Lexicon adopted the 2000 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") to provide for the automatic grant of options to purchase shares of common stock to non-employee directors of the Company. Under the Directors' Plan, non-employee directors first elected after the closing of the Company's initial public offering receive an initial option to purchase 30,000 shares of common stock. In addition, on the date of each of the Company's annual meetings of stockholders, beginning with the annual meeting in 2001, each non-employee director who has been a director for at least six months is automatically granted an option to purchase 6,000 shares of common stock. Initial option grants become vested and exercisable over a period of five years and annual option grants become vested over a period of 12 months from the date of grant. Options granted under the Directors' Plan have an exercise price equal to the fair market value of the Company's common stock on the date of grant and term of ten years from the date of grant.

The Board of Directors initially authorized and reserved a total of 600,000 shares of its common stock for issuance under the Directors' Plan. On the day after each annual meeting of Lexicon's stockholders, for 10 years, starting in 2001, the share reserve will automatically be increased by a number of shares equal to the greater of:

- 0.3% of the Company's outstanding shares on a fully-diluted basis; or
- that number of shares that could be issued under options granted under the Directors' Plan during the prior 12-month period;

provided that the Board of Directors may provide for a lesser increase in the number of shares reserved under the Directors' Plan for any year.

As of December 31, 2002, an aggregate of 600,000 shares of common stock had been reserved for issuance, options to purchase 81,000 shares were outstanding and no options had been exercised under the Directors' Plan.

*Coelacanth Corporation 1999 Stock Option Plan:* Lexicon assumed the Coelacanth Corporation 1999 Stock Option Plan (the "Coelacanth Plan") and the outstanding stock options under the plan in connection with our July 2001 acquisition of Coelacanth Corporation. The Company will not grant any further options under the plan. As outstanding options under the plan expire or terminate, the number of shares authorized for issuance under the plan will be correspondingly reduced.

The purpose of the plan was to provide an opportunity for employees, directors and consultants of Coelacanth to acquire a proprietary interest, or otherwise increase their proprietary interest, in Coelacanth as an incentive to continue their employment or service. Both incentive and nonstatutory options are outstanding under the plan. Most outstanding options vest over time and expire ten years from the date of grant. The exercise price of options awarded under the plan was determined by the plan administrator at the time of grant. In general, incentive stock options have an exercise price of 100% or more of the fair market value of Coelacanth common stock on the date of grant and nonstatutory stock options have an exercise price as low as 85% of fair market value on the date of grant.

As of December 31, 2002, an aggregate of 123,000 shares of common stock had been reserved for issuance, options to purchase 90,000 shares of common stock were outstanding, options to purchase 10,000 shares of common stock had been cancelled and 23,000 shares of common stock had been issued upon the exercise of stock options issued under the Coelacanth Plan.

*Stock-based Compensation:* SFAS 123, "Accounting for Stock-Based Compensation," allows companies to adopt one of two methods for accounting for stock options. Lexicon has elected the method that requires disclosure only of stock-based compensation. Because of this election, the Company is required to account for its employee stock-based compensation plans under APB Opinion No. 25 and its related interpretations. Accordingly, deferred compensation is recorded for stock-based compensation grants based on the excess of the estimated fair value of the common stock on the measurement date over the exercise price. The deferred compensation is amortized over the vesting period of each unit of stock-based compensation grant, generally four years. If the exercise price of the stock-based compensation grants is equal to the estimated fair value of the Company's stock on the date of grant, no compensation expense is recorded.

During the year ended December 31, 2000, Lexicon recorded \$54.1 million in aggregate deferred compensation relating to options issued to employees and non-employee directors. During the years ended December 31, 2002, 2001 and 2000, the Company recognized \$10.3 million, \$10.7 million and \$20.0 million, respectively, in compensation expense relating to these options. Additionally, during the years ended December 31, 2002 and 2001, the Company reversed approximately \$612,000 and \$1.4 million, respectively, of deferred compensation and additional paid-in capital for unamortized deferred compensation related to the forfeiture of nonvested options by terminated employees. Total amortization expense was revised to the extent amortization had previously been recorded for nonvested options.

The pro forma information regarding net loss required by SFAS 123 has been included in Note 2. The information has been determined as if Lexicon had accounted for its employee stock options under the fair-value method as defined by SFAS 123. For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the vesting period of the options using the straight-line method. The fair value of these options was estimated at the date of grant using the Black-Scholes method and the following weighted-average assumptions for 2002, 2001 and 2000:

- volatility factors ranging from 109% to 67%;
- risk-free interest rates of 4.64%, 5.03% and 5.13%, respectively;
- expected option lives of seven years;
- three percent expected turnover; and
- no dividends.

Lexicon records the fair value of options issued to non-employee consultants, including Scientific Advisory Panel members, at the fair value of the options issued. Any expense is recognized over the service period or at the date of issuance if the options are fully vested and no performance obligation exists. No options were issued to non-

employee consultants in 2002. Options to purchase 34,000 and 372,000 shares of common stock were issued to non-employee consultants in 2001 and 2000, respectively. The Company recognized expense relating to options issued to non-employee consultants of \$79,000, \$109,000 and \$836,000 in the years ended December 31, 2002, 2001 and 2000, respectively. The fair values of the issuances in 2001 and 2000 were estimated using the Black-Scholes pricing model with the assumptions noted in the preceding paragraphs, resulting in an aggregate fair value of approximately \$471,000 and \$6.4 million, respectively. Additionally, the Company reversed \$373,000 deferred compensation and additional paid-in capital for unamortized deferred expense primarily related to the forfeiture of nonvested options in the year ended December 31, 2002. Total amortization expense was revised to the extent amortization had previously been recorded for non-vested options.

If vesting continues in accordance with the outstanding individual stock options, Lexicon expects to record amortization expense for deferred stock compensation as follows: \$10.2 million during 2003 and \$884,000 during 2004.

*Stock Option Activity:* The following is a summary of option activity under Lexicon's stock option plans:

	Options Outstanding (In thousands)	Weighted Average Exercise Price
Balance at December 31, 1999 .....	5,197	\$ 1.67
Granted .....	4,464	6.61
Exercised .....	(849)	1.31
Canceled .....	(559)	2.40
Balance at December 31, 2000 .....	8,253	4.33
Granted .....	2,493	11.31
Exercised .....	(419)	1.71
Canceled .....	(224)	9.17
Balance at December 31, 2001 .....	10,103	6.04
Granted .....	2,200	8.68
Exercised .....	(330)	1.74
Canceled .....	(601)	9.70
Balance at December 31, 2002 .....	11,372	6.47
Exercisable at December 31, 2002 .....	7,282	\$ 4.77

The weighted average fair values of options granted during the years ended December 31, 2002, 2001 and 2000 were \$7.32, \$10.31 and \$4.40, respectively. As of December 31, 2002, 2,125,000 shares of common stock were available for grant under Lexicon's stock option plans.

*Stock Options Outstanding:* The following table summarizes information about stock options outstanding at December 31, 2002:

Options Outstanding				Options Exercisable	
Range of Exercise Price	Outstanding as of December 31, 2002 (In thousands)	Weighted Average Remaining Contractual Life (In Years)	Weighted Average Exercise Price	Exercisable as of December 31, 2002 (In thousands)	Weighted Average Exercise Price
\$0.0003 - \$0.22	893	2.9	\$0.05	893	\$0.05
1.67 - 2.50	5,609	6.3	2.41	4,882	2.40
3.35 - 4.99	151	9.5	4.24	18	4.83
5.10 - 7.63	337	9.2	6.33	57	7.07
7.81 - 11.70	2,797	8.8	9.91	592	10.46
11.74 - 16.69	997	8.1	14.05	465	14.15
18.13 - 25.25	384	7.3	20.16	251	20.09
28.69 - 38.50	204	7.7	38.07	124	37.99
	<u>11,372</u>		<u>\$6.47</u>	<u>7,282</u>	<u>\$4.77</u>

#### Warrants

In connection with certain note purchase agreements in August 1997, Lexicon issued two warrants to purchase 13,500 shares and 135,000 shares of common stock at an exercise price of \$2.50 per share. Management estimated



the value of these warrants at approximately \$25,000 and recorded them as deferred financing costs and additional paid-in capital. The warrant values were estimated by management taking into consideration the term of the warrant, the exercise price that was greater than the estimated fair value of the common stock at issuance and a rate of return of eight percent. Amortization of these costs is reflected as additional interest expense in the accompanying financial statements for the year ended December 31, 2000. Both of these warrants were exercised in 2000.

On May 7, 1998, Lexicon issued to the placement agent for the Series A Preferred Stock private placement a warrant to purchase 605,001 shares of common stock at an exercise price of \$2.50 per share. The warrant provided that the exercise price could be paid in cash or by way of a "cashless" exercise based upon the difference between fair market value and exercise price. The value of the warrant, along with the offering costs associated with the private placement, were accreted back to the Series A Preferred Stock through the conversion date of the Series A Preferred Stock. This warrant was exercised in 2001 by way of a cashless exercise, resulting in the issuance of a total of 412,648 shares of common stock.

In July 1998, Lexicon issued a warrant to purchase 249,999 shares of common stock at an exercise price of \$2.50 per share, in connection with the grant to the Company of an option to lease additional real property. The warrant expires on April 15, 2003. Amortization of the remaining balance of \$155,000 on the lease option was expensed in 2000 upon the Company's completion of a synthetic lease agreement under which the lessor purchased the optioned real property under an arrangement providing for its lease to the Company (see Note 10).

In connection with the acquisition of Coelacanth in July 2001, Lexicon assumed Coelacanth's outstanding warrants to purchase 25,169 shares of common stock. The warrants expire on March 31, 2009. The fair value of the warrants was included in the total purchase price for the acquisition. As of December 31, 2002, warrants to purchase 16,483 shares of common stock, with an exercise price of \$11.93 per share, remained outstanding.

#### *Aggregate Shares Reserved for Issuance*

As of December 31, 2002, an aggregate of 11,639,000 shares of common stock were reserved for issuance upon exercise of outstanding stock options and warrants and 2,124,000 additional shares were available for future grants under Lexicon's stock option plans.

### **13. Benefit Plans**

Lexicon has established an Annual Profit Sharing Incentive Plan (the Profit Sharing Plan). The purpose of the Profit Sharing Plan is to provide for the payment of incentive compensation out of the profits of the Company to certain of its employees. Participants in the Profit Sharing Plan are entitled to an annual cash bonus equal to their proportionate share (based on salary) of 15 percent of the Company's annual pretax income, if any.

Lexicon maintains a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all full-time employees. Participating employees may defer a portion of their pretax earnings, up to the Internal Revenue Service annual contribution limit. Beginning in 2000, the Company was required to match employee contributions according to a specified formula. The matching contributions totaled approximately \$645,000, \$332,000 and \$160,000 in 2002, 2001 and 2000, respectively. Company contributions are vested based on the employee's years of service, with full vesting after four years of service.

### **14. Collaboration and License Agreements**

Lexicon derives substantially all of its revenues from subscriptions to its databases, drug discovery alliances, functional genomics collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses and compound library sales.

*Drug Discovery Alliances:* Lexicon has entered into the following alliances for the discovery and development of therapeutics based on its *in vivo* drug target discovery efforts:

*Abgenix, Inc.* Lexicon established a drug discovery alliance with Abgenix in July 2000 to discover novel therapeutic antibodies using the Company's functional genomics technologies and Abgenix's technology for generating fully human monoclonal antibodies. Lexicon and Abgenix expanded and extended the alliance in January 2002, with the intent of accelerating the selection of *in vivo*-validated antigens for antibody discovery and the development and commercialization of therapeutic antibodies based on those targets. Under the alliance agreement, the Company and

Abgenix will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic antibodies, and will each receive milestone payments and royalties on sales of therapeutic antibodies from the alliance that are commercialized by the other party or a third party sublicensee. Each party will bear its own expenses under the alliance. The expanded alliance also provides us with access to Abgenix's XenoMouse® technology for use in some of our own drug discovery programs. The agreement, as extended, has a term of four years, subject to the right of the parties to extend the term for up to three additional one-year periods.

*Genentech, Inc.* Lexicon established a drug discovery alliance with Genentech in December 2002 to discover novel therapeutic proteins and antibody targets. Under the alliance agreement, Lexicon will use its functional genomics technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Genentech will have exclusive rights in the discoveries resulting from the collaboration for the research, development and commercialization of therapeutic proteins and antibodies. Lexicon will retain certain other rights in those discoveries, including rights for the development of small molecule drugs. Lexicon received an upfront payment and funding under a loan in 2002, and will receive performance payments for its work in the collaboration as it is completed. The terms of the loan are discussed in Note 9. Lexicon will also receive milestone payments and royalties on sales of therapeutic proteins and antibodies for which Genentech obtains exclusive rights. The agreement has an expected collaboration term of three years.

*Incyte Genomics, Inc.* Lexicon established a drug discovery alliance with Incyte in June 2001 to discover novel therapeutic proteins using the Company's functional genomics technologies in the discovery of the functions of secreted proteins from Incyte's LifeSeq® Gold database. Under the alliance agreement, the Company and Incyte will each have the right to obtain exclusive commercialization rights, including sublicensing rights, for an equal number of qualifying therapeutic proteins, and will each receive milestone payments and royalties on sales of therapeutic proteins from the alliance that are commercialized by the other party or a third party sublicensee. The agreement has a term of five years, although either party may terminate the agreement after three years.

*LexVision Collaborations:* Lexicon has entered into the following collaborations for access to the Company's LexVision database of *in vivo*-validated drug targets:

*Bristol-Myers Squibb Company.* Lexicon established a LexVision collaboration with Bristol-Myers Squibb in September 2000, under which Bristol-Myers Squibb has non-exclusive access to the Company's LexVision database and OmniBank library for the discovery of small molecule drugs. The Company receives access fees under this agreement, and is entitled to receive milestone payments and royalties on products Bristol-Myers Squibb develops using the Company's technology. The agreement has a term of five years, although either party may terminate the agreement after three years.

*Incyte Genomics, Inc.* Lexicon established a LexVision collaboration with Incyte in June 2001, under which Incyte has non-exclusive access to the Company's LexVision database and OmniBank library for the discovery of small molecule drugs. The Company receives access fees under this agreement, and is entitled to receive milestone payments and royalties on products Incyte develops using the Company's technology. The agreement has a term of five years, although either party may terminate the agreement after three years.

#### 15. Selected Quarterly Financial Data

The table below sets forth certain unaudited statements of operations data, and net loss per common share data, for each quarter of 2002 and 2001.

(In thousands, except per share data)

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(Unaudited)			
<b>2002</b>				
Revenues.....	\$ 7,656	\$ 9,411	\$ 8,013	\$ 10,120
Loss from operations .....	(15,177)	(15,640)	(17,491)	(14,585)
Net loss .....	(14,059)	(14,940)	(16,809)	(13,862)
Net loss per common share, basic and diluted.....	(0.27)	(0.29)	(0.32)	(0.26)
Shares used in computing net loss per common share.....	52,126	52,250	52,314	52,357

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(Unaudited)			
<u>2001</u>				
Revenues.....	\$ 3,311	\$ 3,502	\$ 13,493	\$ 10,271
Loss from operations .....	(10,823)	(12,236)	(7,955)	(12,625)
Net loss .....	(8,008)	(9,939)	(6,220)	(11,005)
Net loss per common share, basic and diluted.....	(0.17)	(0.20)	(0.12)	(0.21)
Shares used in computing net loss per common share.....	48,343	48,865	51,500	51,955

*executive* OFFICERS

**Arthur T. Sands, M.D., Ph.D.**

President and Chief Executive Officer

**Julia P. Gregory**

Executive Vice President and Chief Financial Officer

**Jeffrey L. Wade, J.D.**

Executive Vice President and General Counsel

**Brian P. Zambrowicz, Ph.D.**

Executive Vice President of Research

**Walter F. Colbert**

Senior Vice President of Human Resources  
and Corporate Services

**Alan J. Main, Ph.D.**

Senior Vice President of Lexicon Pharmaceuticals

**James R. Piggott, Ph.D.**

Senior Vice President of Pharmaceutical Biology

**Randall B. Riggs**

Senior Vice President of Business Development

**David A. Boulton**

Vice President of Technology Operations,  
Lexicon Pharmaceuticals

**Lance K. Ishimoto, J.D., Ph.D.**

Vice President of Intellectual Property

**David Kimball, Ph.D.**

Vice President of Medicinal Chemistry

**Stephen J. McAndrew, Ph.D.**

Vice President of Pharmaceutical Business Development

**Christophe Person**

Vice President of Informatics

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**Arthur T. Sands, M.D., Ph.D.**

President and Chief Executive Officer,  
Lexicon Genetics Incorporated

This annual report to shareholders contains forward-looking statements. These statements involve risks, uncertainties and other important factors that may cause the actual results of Lexicon to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such risks, uncertainties and other important factors is contained in the sections entitled "Factors Affecting Forward-Looking Statements" and "Business - Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2002, as filed with the Securities and Exchange Commission and included as part of this annual report to shareholders.

*corporate* INFORMATION

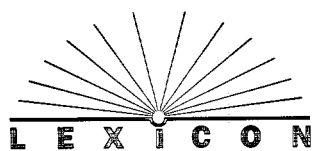
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Our 2002 annual report on Form 10-K is available, without charge, upon request by contacting our Corporate Communications Department at 281-863-3000.

Our annual meeting of shareholders will be held at 1:30 p.m. CDT on April 30, 2003 at the Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas 77380.

Visit our corporate website at  
<http://www.lexicon-genetics.com>.



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